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SEE PAGE 15

EM CASES

MANAGEMENT
PEARLS AND
PITFALLS IN SICKLE
CELL DISEASE
SEE PAGE 20

SKEPTICS' GUIDE TO EMERGENCY MEDICINE

AMIODARONE,
LIDOCAINE, OR
PLACEBO IN OHCA?
SEE PAGE 25



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Extended-Spectrum Beta-Lactamase Infections: COMING SOON TO YOUR COMMUNITY

*Choosing the right medication combination for this
emerging superbug is critical to good outcomes*

by DAVID A. TALAN, MD, FACEP, FAAEM, FIDSA

HAVE YOU WONDERED when you'd start to routinely confront superbugs resistant to multiple antibiotics in your emergency department and not just in grocery line tabloids? Unfortunately, the time has come, and without awareness, some of our patients will have bad outcomes because of undertreatment.

CONTINUED on page 13



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A NEW SPIN

ACA AND CONSOLIDATION

*Obamacare is increasing
health plans' market power*

by ED GAINES, JD, CCP

*"The opportunity to secure ourselves
against defeat lies in our own hands,
but the opportunity of defeating the
enemy is provided by the enemy him-
self."—Sun Tzu*

Since the enactment of the Affordable Care Act (ACA) on March 23, 2010, and the creation of commercial health exchanges, there has been a growing stream (that has now become a torrent) of health plans leaving the exchanges. The insurance exchanges are where health plans like Blue Cross Blue Shield, Aetna, and UnitedHealthcare (UHC) have sold subsidized health care policies to individuals pursuant to the insurance mandates of the ACA. Citizens between 138 and 400 percent of federal poverty level (FPL) receive premium subsidies, and there are cost-sharing subsidies for folks who are at or below 250 percent of FPL. (Premium subsidies continue for folks from 250 percent of FPL up to a maximum of 400 percent of FPL, while the cost sharing [eg, coinsurance and deductible] subsidies phase out at above 250 percent of FPL.)

Also consider as an overall environmental assessment the full frontal assault by these same health plans at the federal and state level to ban or severely restrict out-of-network (OON) balance billing by hospital- and clinic-based physicians and in some cases specifically targeting emergency physicians.

You might be tempted to ask, how are the health plans' participation (or lack thereof) in the ACA exchanges

CONTINUED on page 4

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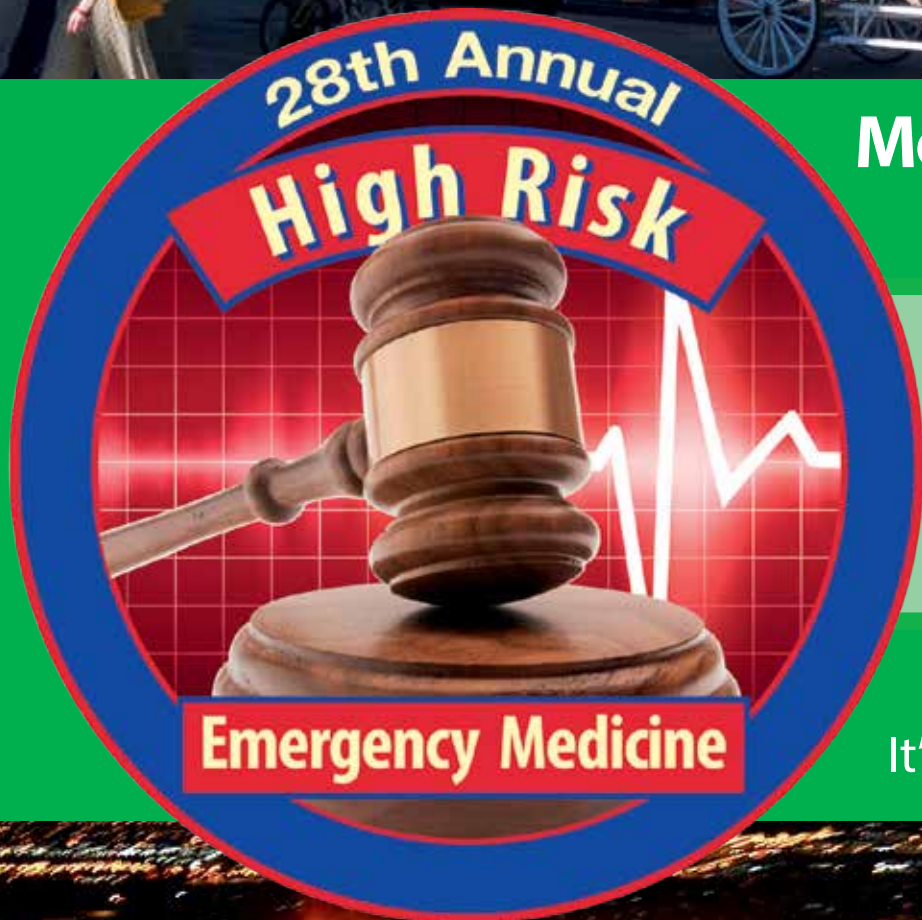
New ACEP Clinical Policy on Transient Ischemic Attack

SEE PAGE 12

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NEWS FROM THE COLLEGE

ACEP16 ROUNDUP



New Leadership, Exceptional Attendance Highlight ACEP16

Records were shattered in Las Vegas at ACEP16, with 7,513 emergency physicians and other health care providers attending the full four-day meeting, the world's largest emergency medicine educational conference.

New leadership was also elected during the meeting in October. A new President-Elect and four members of the Board of Directors were elected by the ACEP Council. Contributions to the National Emergency Medicine Political Action Committee (NEMPAC) and the Emergency Medicine Foundation (EMF) were also higher than expected with the conference's large turnout. Such contributions will result in a stronger voice

"ACEP needs strong leaders who understand business models, the practice challenges, the political environment, and have the ability to advocate, consensus build, and communicate the value of emergency medicine."

—Dr. Kivela

for advocacy in Washington and further pursuit of emergency medicine research.

Incoming ACEP President Rebecca Parker, MD, FACEP, took the reins of ACEP in Las Vegas as Paul Kivela, MD, MBA, FACEP, was elected as ACEP President-elect.

Dr. Kivela, managing partner of Napa Valley Emergency Medical Group and medical director of Medic Ambulance in Vallejo, California, will assume the presidency at ACEP17 in Washington, D.C.

"The only thing that is certain is that the practice of emergency medicine will look different in the future," Dr. Kivela said. "To meet the challenges, ACEP needs strong leaders who understand business models, the practice challenges, the political environment, and have the ability to advocate, consensus build, and communicate the value of emergency medicine."

The Council reelected incumbent Board of Directors members James J. Augustine, MD, FACEP, and Debra G. Perina, MD, FACEP. The Council also voted in two new Board members: Kevin M. Klauer, DO, EJD, FACEP, and Gillian Schmitz, MD, FACEP.

NEMPAC

As in years past, ACEP Council members stepped up to the plate during the NEMPAC Council Challenge to ensure that emergency medicine stays among the top of the leaderboard among medical PACs and continues to be a strong, respected voice in Washington, D.C.

Prior to and during the ACEP Council meeting, NEMPAC collected nearly \$300,000 from Council members. That combined with thousands of donations this year from ACEP members across the country means NEMPAC is well on its way to exceeding the \$1 million goal set by the ACEP Board of Directors in 2016. Along with more than \$1 million collected from ACEP members last year, NEMPAC was able to contribute \$1.8 million to 26 Senate candidates and 208 House races.

NEMPAC serves a vital role in advancing ACEP's legislative agenda and in broadening ACEP's visibility with Congress. NEMPAC's growth has allowed us to impact more congressional races for candidates supportive of emergency medicine and ACEP and has expanded our influence on Capitol Hill.

Emergency Medicine Foundation

The EMF surpassed its goal for the second year with Council Challenge at ACEP16 in Las Vegas. The challenge drew \$223,000 in contributions, exceeding the \$220,000 goal for the year. The average contribution approached the recommended new "Wilcox" level of \$600, with a record number of contributors stepping up to become major donors and 1972 Club members.

EMF is continuing its Pave the Way campaign through Dec. 31, giving members a final opportunity to purchase a brick paver to help build the future of the specialty by donating a personalized brick paver at ACEP's headquarters. ☺



A NEW SPIN: ACA AND CONSOLIDATION | CONTINUED FROM PAGE 1

and the largely state-level efforts to ban and/or restrict OON balance billing related? Although it may seem that we're talking about two different subjects, they're more closely intertwined than you might think.

STAYING "IN NETWORK"

Let's take one case in point: Aetna's announcement on Aug. 15, 2016, that it will withdraw from 11 of 15 states where it participates in the ACA exchanges.

In July 2015, Aetna announced that it would purchase Humana in a \$37 billion cash and stock deal. In April 2016 while on a quarterly earnings conference call with analysts, Aetna CEO Mark Bertolini said of the ACA exchanges, "We see this as a good investment." In May, Bertolini reiterated that Aetna planned to stay in the exchanges in response to questions regarding UHC's decision to leave the exchanges in 2017.

After being asked to respond, however, Bertolini wrote to the US Department of Justice (DOJ) on July 5, 2016, saying, "If the DOJ sues to enjoin the transaction [with Humana], we will immediately take action to reduce our 2017 exchange footprint."¹ (Under the federal anti-trust laws, the DOJ and the Federal Trade Commission have jurisdiction to review, revise, and/or legally oppose mergers and acquisitions.)

Now let's look at the dynamics from the larger perspective of the United States as a whole. According to a report from Aug. 19, 2016, in *The New York Times* and an analysis that the *Times* commissioned, there is exactly one ACA health plan selling policies in the exchanges in Alaska, Arkansas, Kansas, Oklahoma, South Carolina, and Wyoming. While small portions of these states have more than one plan, Missouri, North Carolina, Tennessee, Utah, and West Virginia have largely one ACA health plan per state.² In contrast, in 2016, Wyoming and most of Utah had only one ACA plan. So what does that mean for the future of the ACA and the future of the broader health plan agenda?

The health plans can and will leverage their positioning in the exchanges on future federal and state administrations in an attempt to make OON balance billing prohibited by federal fiat (a legal, authoritative decision that has absolute sanction), as the Obama administration threatened to do in November 2015.

USING LEVERAGE

Much of it depends on the outcome of the presidential election. Hillary Clinton seeks to expand and defend the ACA, according to her policy papers on her website and her public statements. According to independent analyst Charles Gaba, the national average year-over-year (YOY) requested ACA premium increase is 23.9 percent for 2017.³ What would occur in the future if the health plans remaining in the exchanges didn't receive their YOY premium increase requests from the Centers for Medicare & Medicaid Services (CMS) and state insurance officials?

The answer is that the health insurance exchanges would collapse, barring federal intervention—and isn't that begging the question for the future of a single-payer system? The cynic would say that this was the goal all along: Make it look like a market-based solution for a few years and then sweep in with the "Medicare for all" proposal.

Finally, the dynamics of the ever-growing leverage a small number of health plans has over political leaders has major impact on the OON issues. The health plans can and will

leverage their positioning in the exchanges on future federal and state administrations in an attempt to make OON balance billing prohibited by federal fiat (a legal, authoritative decision that has absolute sanction), as the Obama administration threatened to do in November 2015.⁴ Aetna proved this summer that it wasn't below "leveraging" (threatening) the administration. Aetna has also been one of the loudest voices to drive OON reimbursement to at or about 125 percent of the Medicare fee schedule in states considering OON restrictions.

The collective opposition from ACEP, the Emergency Department Practice Management Association (EDPMA), and the new Physicians for Fair Coverage against further health plan consolidation, flexing their market power, and "lose-lose" health plan OON proposals will have to make the difference in several areas: 1) drafting model OON legislation with minimum benefit standards tied to fair health; 2) establishing or supporting existing multispecialty physician coalitions to enact that legislation, including local fundraising to support government relations (GR) and public relations (PR) initiatives; and 3) developing and launching PR and GR strategies to oppose health plans' messaging and enact that proposed legislation. ☛

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MR. GAINES is chief compliance officer, emergency medicine division, at Zotec Partners, LLC, based in Greensboro, North Carolina. He is also chair of the ACEP/EDPMA Joint Task Force on Reimbursement Issues, which cover both OON and Medicaid issues.

"A New Spin" is the personal perspective of the author and does not represent an official position of ACEP Now or ACEP.





by ERIC J. MORLEY, MD, MS, *department of emergency medicine, Stony Brook School of Medicine, New York*

FDA Requires Boxed Warning, Medication Guides for Opioids, Benzodiazepines

The prescription of opioids and benzodiazepines in combination has increased 41 percent between 2002 and 2014. The FDA will now be mandating “boxed warnings” on 389 separate products in an effort to decrease this dangerous combination.

“A Hopeful Sign”: Experimental Alzheimer’s Drug Shows Promise

A monoclonal antibody that targets amyloid plaques seen in Alzheimer’s shows promise in slowing the typical decline observed with this disease. Hopefully, phase III studies will prove this drug to be beneficial.

Researchers Find Association Between Zika and Guillain-Barre Syndrome

The Zika virus has largely been considered a fairly benign viral illness for men and non-pregnant females. However, a recent case series published in The New England Journal of Medicine indicates that the

incidence of Guillain-Barre syndrome is 2.0–9.8 times higher than baseline in seven Latin American and Caribbean countries, and this appears to correlate with Zika infections.

Massachusetts Sees Consultant Availability Decrease Between 2005 and 2014

A recent study in the Annals of Emergency Medicine found a decrease in the availability of many specialty consultants in emergency departments across Massachusetts between 2005 and 2014 despite steadily increasing patient visits. General surgery, neurology, ob-gyn, orthopedics, pediatrics, plastic surgery, and psychiatry were the specialties that saw a decrease.

Illinois Sees Increase in ED Visits After Rollout of Affordable Care Act

A study published in the Annals of Emergency Medicine shows emergency department visits have increased since the implementation of the Affordable Care Act despite no increased rate of hospitalization. It is unclear if these visits were unnecessary and better suited for the primary care setting. ➔

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To Manage Hospital Crowding, Look Beyond the ED

The trick to smoothing patient flow is found outside of the emergency department

Many hospitals in the country operate at capacity, and many patients are boarded in the emergency department. Although there are many ED-based flow initiatives, virtually none of these address the most significant impediment to flow: boarding of admitted patients in the emergency department due to lack of inpatient beds. Only a few interventions really have any lasting and significant impact on boarding and capacity.

This is one of a series of interviews that highlight dramatically effective interventions to reduce boarding and crowding. Eugene Litvak, PhD, is a world-renowned expert in hospital flow who made the remarkable discovery that our problem with capacity is driven in large part by elective scheduling, not by ED admissions. We sat down to discuss his experiences tackling the issue of hospital crowding.

PARTICIPANTS



Peter Viccellio, MD, FACEP, is vice chairman of the department of emergency medicine and associate chief medical officer for the Health Sciences Center at Stony Brook University in New York.



Eugene Litvak, PhD, is president and CEO of the Institute for Healthcare Optimization and an adjunct professor in operations management at the Harvard School of Public Health in Boston.

PV: This is one of a series discussing hospital and ED crowding and its impact on patient safety, finance, and staffing. How did you get into the whole arena of hospital capacity and flow?

EL: I came to this country in 1988 from the former Soviet Union. I already had dozens of publications in the United States, and many of my colleagues recommended that I should go anywhere but health care because in this industry, efficiency is not a goal; there is no interest to increase efficiency. That was a red flag for me. I started doing some limited consulting at hospitals and started trying to learn the environment at the hospital, working with the frontline people, ie, nurses, physicians, etc. At that point, I met Dr. Michael Long, an anesthesiologist. At that point, the question that we were trying to address was, what happens with hospitals overcrowding? We found that at the same time hospitals are getting more and more overcrowded, the hospitals' census and bed occupancy experienced large fluctuations. My initial belief was that everything stemmed from the emergency department. There are two main portals to any

hospital. Emergency departments are responsible for over 50 percent of all admissions, and there are elective admissions, mostly surgical, typically responsible for up to 30–35 percent of admissions, the remaining admissions being medical referrals, transfers, etc.

PV: So your first assumption was that this was due to influx of emergency patients?

EL: Absolutely. It was based on the common sense for two reasons: First, the volume is the highest among all admits, and second, it's unpredictable by its nature. Elective admissions are smaller in terms of the volume, and their schedule is up to us. Unfortunately, our health care delivery is not always based on common sense.

PV: What did you find?

EL: It was impossible for Dr. Long and me to get the data from emergency departments. Nobody wanted to share the data with us. However, we were able to get the data from one operating room. Two transparencies were on the desk in front of us. One of them was bed occupancy, and the other was surgical volume. We found they were overlapping. They had about the same shape. So if you put it up to the window glass and overlap one over another to compare, we found that they practically coincided. That was for me a real aha moment: Emergency department admissions had very little to do with variability. Since then, for years I have talked to many hospital emergency department leaders asking, "Five Tuesdays from now, short of a bus crash or flu epidemic, could you predict approximately how many patients are going to be admitted to your emergency department?" The answer was always yes. Then I asked many operating room managers the same question: "Five weeks from now on Tuesday, how many surgeries are you going to perform?" Given that typically over 70 percent of all surgeries performed are elective, I was very surprised to find out that people cannot answer this question. That, to me, was clear evidence regarding the source of this variability. Of course, this was not just the surgical admissions. This is true for the other elective admissions, eg, cath lab.

PV: Do you find this to be true at most institutions?

EL: Practically everywhere. In dozens of hospitals where I asked this question, the answer was the same. It's not just in the United States. It's true in Europe, Canada, you name it. It looks like an international plot against health care cost and quality and the main driver of capacity problems.

PV: In response to this, there were three things that were implemented that we

refer to as smoothing: separating out the emergency surgical flow from the elective surgical flow, smoothing the number of surgeries over the week, and also smoothing them to predict the number of ICU beds needed.

EL: That is absolutely correct. Moreover, I would say that's not *an* intervention. That is *the* intervention. We have only two options. The first option is to provide excessive resources to staff at the peak level, which no hospital in the world has resources to do. The other choice is to staff below the peak level, a pivotal way of staffing hospital wards today. Typically, we staff them at the average level that has been documented historically from the last year. About 10 years ago, we received a grant from the Robert Wood Johnson Foundation to study two community and two academic hospitals, and we found that ward bed occupancies changed every hour, if not every half hour. There is absolutely no way that one may have a pool of nurses dynamic enough to address heavy peak volumes because nurses do not live in the hallway to address every hour or half-hour change in the census.

PV: In the places where you helped to implement smoothing of the elective schedule, what was the end result?

EL: The end result was huge, both financial and quality wise at every hospital. Cincinnati Children's is probably one of the most impressive examples. When we started working with them on smoothing, their census was at the 76 percent level. In order to address peaks, they planned to build a new tower for \$100 million in capital costs. Each bed in the United States, in terms of the capital cost, varies from \$1.5 million to \$3 million in capital cost alone. Plus, the annual operational cost *per bed* is at least half a million dollars. At the end of our smoothing project, they abandoned their plan to build the new tower. The average census reached 91 percent, a 15 percent increase. Their surgical volume increased dramatically without capacity issues because when we cut off the peak, we filled up the valley. It's not just the peaks that create quality consequences; when we have those valleys, that's a waste of our resources. Their surgical volume dramatically increased, and according to their report, their margin improved by over \$100 million a year. It's not just \$100 million in avoided capital cost; it's an additional over \$100 million a year margin improvement and quality improvement.

PV: I understand that hospitals had had significant problems with boarding in the emergency department that also disappeared as soon as they smoothed their capacity.

CONTINUED on page 11

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ACEP Council Reviews Public Policy and Various Resolutions at Annual Meeting

LAS VEGAS—The 2016 ACEP Council considered several resolutions during its annual meeting in October, including issues related to public policy, clinical issues, and emergency medicine practice trends.

This year's 392-member Council represented all 53 chapters, 33 ACEP sections of membership, the Emergency Medicine Residents' Association (EMRA), the Association of Academic Chairs in Emergency Medicine, the Council of Emergency Medicine Residency Directors, and the Society of Academic Emergency Medicine.

The resolutions adopted by the Council became College policy after they are reviewed and approved by the ACEP Board of Directors.

The Council considered, but ultimately did not adopt, a resolution to support the establishment of a full-voting young physician position on the ACEP Board of Directors.

The Council was divided on this issue, with those in favor saying a designated position would bring generational diversity and a different energy, while engaging younger physicians. Those opposed stated that a particular demographic should not be singled out and that efforts could be made to get younger physicians on the slate of candidates.

The Council also considered a resolution to oppose "required high stakes secured examination(s) for Maintenance of Certification." After spirited discussion on both sides of the resolution, the Council decided to refer it to the Board of Directors.

THE COUNCIL ADOPTED RESOLUTIONS RELATED TO:

- Accreditation standards for freestanding emergency centers
- Assuring safe and effective care for patients by senior/late career physicians
- Best practices for harm reduction strategies
- Boating and overcrowding is a public health emergency
- Centers of Medicare & Medicaid Services (CMS) recognition of independently licensed freestanding emergency centers
- Court-ordered forensic evidence collection in the ED
- Development and application of dashboard quality clinical data related to the management of behavioral health patients in EDs
- Diversity in emergency medicine leadership
- Enactment of narrow networks requirements
- Freestanding emergency centers as a care model for maintaining access to emergency care in underserved and rural areas of the US
- Health care financing task force
- Legacy fellows (bylaws housekeeping)
- Medication-assisted therapy for patients with substance use disorders in the emergency department

- Mental health boarding solutions
- Military medics integration into civilian EMS
- Opposing the development of sublingual sufentanil
- Opposition of exclusive imaging contracts limiting clinical ultrasound use and billing by emergency physicians
- Opposition to CMS mandating treatment expectations
- Pediatric surgery centers
- Reimbursement for opioid counseling
- Support and advocacy for 24/7 hyperbaric medicine availability
- The opioid epidemic—a leadership role for ACEP

THESE ITEMS WERE REFERRED TO BOARD FOR ADDITIONAL CONSIDERATION:

- Collaboration with non-medical entities on quality and standards
- Criminal justice reform—national decriminalization of possession of small amounts of marijuana for personal use
- Insurance collection of beneficiary deductibles
- Treatment of marijuana intoxication in the emergency department

Next year's Council meeting will take place Oct. 28–29 in Washington, D.C. 📍

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Recommendations for ED Thoracotomy from EAST

Eastern Association for the Surgery of Trauma guidelines note when ED thoracotomy makes sense and when it does not

by GRAHAM INGALSBE, MD, AND STEPHEN WOLF, MD, FACEP

The ACEP Clinical Policies Committee regularly reviews guidelines published by other organizations and professional societies. Periodically, new guidelines are identified on topics with particular relevance to the clinical practice of emergency medicine. This article highlights recommendations on the indications for emergency department thoracotomy from the Eastern Association for the Surgery of Trauma (EAST) published in the *Journal of Trauma and Acute Care Surgery* in 2015.

“Stab wound to the chest, CPR in progress, three minutes out!”

You stop what you’re doing on a busy shift and head to the trauma bay. The room quickly becomes abuzz with nurses, techs, and respiratory therapists preparing for an injured trauma patient. Trauma blood arrives. You prepare your airway tools, line up your procedure trays, and assign roles to the members of your team. Suddenly, the paramedic crew rushes into the room with compressions under way; they lost pulses approximately eight minutes prior. The trauma team is scrubbing out of a case and won’t be down for five minutes. What do you do?

Few procedures in emergency medicine evoke more heated controversy than that of the resuscitative thoracotomy. Often a last-resort Hail Mary procedure, opening a chest in the emergency department is never taken lightly. Variations in practice across the country prompted EAST to pore over existing data and make specific recommendations for when it’s most appropriate (or not) to consider performing an emergency thoracotomy.

METHODOLOGY

The authors, composed mostly of trauma surgeons and one emergency physician, used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology for a systematic review and developed six population, intervention, comparator, and outcomes (PICO) questions. A systematic search using PubMed and Embase databases was performed using the following combination of medical subject headings terms and related key words: thoracotomy, emergency medical services, emergency treatment, emergencies, emergency room, emergency department, emergency service, and emergency ward. Only studies published in English were included. Exclusion criteria were meta-analyses, reviews without original data, case reports, letters, and studies that involved either pre-hospital or operating room thoracotomy.

The questions developed cover specific traumatic scenarios, including penetrating thoracic trauma, penetrating extra-thoracic trauma, and blunt trauma with or without signs of life.

Often a last-resort Hail Mary procedure, opening a chest in the emergency department is never taken lightly. Variations in practice across the country prompted EAST to pore over existing data and make specific recommendations for when it’s most appropriate (or not) to consider performing an emergency thoracotomy.

A comparator was necessary for the PICO format. (Studies with an active comparator compare the treatment with another treatment commonly used for the same indication, rather than with no treatment, to help limit bias.) Interestingly, as no such comparator could be identified for patients who had *not* undergone ED thoracotomy, the guideline developers estimated baseline survival using a poll of panel members who were provided trauma scenarios treated without ED thoracotomy (eg, intravenous access, blood product resuscitation, thoracostomy tube placement, and transfer to the operating room). High and low outliers were excluded, and the remaining predicted outcomes were averaged to give a comparator survival percent.

RECOMMENDATIONS

Each guideline recommendation is presented below with highlighted corroborating data and discussion pertinent to emergency physicians.

1 In patients who present pulseless to the emergency department *with signs of life* after *penetrating thoracic injury*, EAST **strongly recommends** resuscitative ED thoracotomy.

- This is the only recommendation considered *strong* in this guideline, based on patient preference for improved chance of survival and a moderate quality of evidence (21.3 percent survival among 853

patients, of which 90 percent were neurologically intact).

2 In patients who present pulseless to the emergency department *without signs of life* after *penetrating thoracic injury*, EAST **conditionally recommends** resuscitative ED thoracotomy.

- This is based on patient preference and moderate overall quality of evidence (8.3 percent survival based on 920 patients in 32 studies). Among the 641 patients in whom neurologic outcome was reported, 3.9 percent survived neurologically intact.
- Length of CPR time as a factor to consider was discussed within this clinical question. The authors concede that data are lacking to give exact durations for traumatic CPR arrest. However, the authors stated, “We are unable to offer any alteration to the commonly held dictum: ED thoracotomy is likely futile after 15 minutes of arrest time after penetrating injury.”

3 In patients who present pulseless to the emergency department *with signs of life* after *penetrating extra-thoracic injury*, EAST **conditionally recommends** resuscitative ED thoracotomy.

- There was a small patient population that provided data for this clinical scenario. Among the 160 patients in 11 studies, there was a 15.6 percent survival rate. Neurologic outcomes were cited in only 85 patients; 16.5 percent survived intact.

4 In patients who present pulseless to the emergency department *without signs of life* after *penetrating extra-thoracic injury*, EAST **conditionally recommends** resuscitative ED thoracotomy.

- Survival was 2.9 percent among this small data set of 139 patients from eight studies. Neurologic outcome was reported for 60 patients, and only three of those survived neurologically intact.

5 In patients who present pulseless to the emergency department *with signs of life* after *blunt injury*, EAST **conditionally recommends** resuscitative ED thoracotomy.

- Survival was 4.6 percent among 454 patients in 22 studies. Neurologic outcome was reported in 298 of these patients, and only 2.4 percent survived ED thoracotomy neurologically intact.

6 In patients who present pulseless to the emergency department *without signs of life* after *blunt injury*, EAST

conditionally recommends against resuscitative ED thoracotomy.

- This was the only conditional recommendation *against* the procedure.
- Survival was 0.7 percent based on data from 995 patients in 24 studies. Neurologic outcome in 825 patients showed only 0.1 percent surviving neurologically intact (one patient out of 825).

LIMITATIONS AND DISCUSSION

- Data are mostly from Level I trauma centers, and the authors concede that these guidelines may not be applicable to smaller, community, or rural centers with fewer operative resources.
- While the term “neurologically intact” was used repeatedly throughout the guideline, this term was not clearly defined.
- “Signs of life” were defined by the authors as pupil response, spontaneous ventilation, presence of carotid pulse, measurable or palpable blood pressure, extremity movement, or cardiac electrical activity. These may be controversial and not universally applied to all studies. Some providers may also not consider cardiac electrical activity alone (or pulseless electrical activity) as a true sign of life.
- The authors of the guideline note that all of the studies that inform the recommendations have serious limitations.
- The risk to providers while performing ED thoracotomy was discussed, including concerns of bloodborne pathogens and risk of provider injury. These should be taken into consideration with this highly invasive procedure.

CONCLUSIONS

Guidelines aren’t meant to replace clinical judgment but rather to augment the decision-making process. As with much of medicine, there’s always a need for more and better data, and this set of recommendations is no exception. The decision to perform an ED thoracotomy depends heavily on the institutional setting and the downstream resources available to the emergency physician. ☛

Reference

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DR. INGALSBE is chief resident at the Denver Health Residency in Emergency Medicine in Colorado. **DR. WOLF** is associate professor of emergency medicine at the University of Virginia School of Medicine in Charlottesville.

TO MANAGE HOSPITAL CROWDING, LOOK BEYOND THE ED | CONTINUED FROM PAGE 6

EL: Boston Medical Center is a Level I trauma center. Their emergency department was constantly overloaded. After surgical smoothing, their ambulance diversion decreased by 20 percent. Their waiting time dropped to 2.8 hours compared to five plus hours at other academic hospitals in Boston. Improvement in the emergency department overcrowding was not at the expense of the surgeon. Due to their nature of being a Level I trauma center, their cases were frequently bumped by the emergent surgeries with gunshots, etc. The number of cancelled or rescheduled cases dropped by 99.5 percent, from the average of 700 a year to about six a year.

PV: What are the upsides and the downsides?

EL: Ottawa Hospital is a large academic hospital. They reported a \$9 million margin improvement, and they reported 40 lives were saved in the first year. Why? Because they documented that when the hospital is overcrowded and the operating rooms are overcrowded, the waiting time to get emergent or urgent surgery could become prohibitive, resulting in an increased mortality rate.

PV: Hospitals are doing so many different things to address crowding. Few have been effective or sustained. Would you consider this intervention just one of many on the list of things that hospitals can do?

EL: As long as we have those peaks, we are going nowhere. Let me give you another example from 2009 publication in *Critical Care Medicine*. At the Johns Hopkins neurological ICU, authors found that during peaks in admissions, the hospital readmission rate increased by 500 percent. What does that mean? I believe that [the Centers for Medicare & Medicaid Services] suggest that there should be a 20 percent reduction in the hospital readmission. If you do not smooth, you could report a success, with 400 percent instead of 500 readmission rate during those peak days. When I say that Cincinnati Children's was able to improve their margin by \$100 million a year, hospitals of similar size that do not do that will waste \$100 million a year. In terms of safety, cost, readmission rates, and mortality rates, it's dangerous to the patient and the financial well-being of the hospital to ignore these peaks and troughs. I consider this an absolutely essential part of any effort to address crowding. Without it, you will not solve your problem.

PV: In summary, you have found that smoothing improves the hospital's available capacity to decrease emergency department boarding of admitted patients, and you're going to have steadier nurse-patient ratios without peaks and valleys. It's going to be safer for the patients, it's going to be better for the hospital's financial line, and it's going to actually be better for the doctors, particularly those that are doing elective surgery, because they don't get their cases bumped, their patients are placed in the preferred rooms, and one can run the elective operating room with a higher capacity because it's much more predictable.

"When I say that Cincinnati Children's was able to improve their margin by \$100 million a year, hospitals of similar size that do not do that will waste \$100 million a year. In terms of safety, cost, readmission rates, and mortality rates, it's dangerous to the patient and the financial wellbeing of the hospital to ignore these peaks and troughs. I consider this an absolutely essential part of any effort to address crowding. Without it, you will not solve your problem."

—Eugene Litvak, PhD

EL: That is absolutely correct. So what is the alternative today? Let's build more beds. The average hospital bed occupancy in the United States is much lower than in any industrialized countries. In the US, it's about 66 percent on average. One-third of our hospitals are empty, and yet we are overcrowded. That's everyday life compared to Canada, for example, when their average bed occupancy is 90 percent. We have this luxury of having a lot of beds, and yet we are overcrowded. Building more beds would not solve the problem.

PV: Some hospitals reading this will say, though, that they run at an average occupancy of 85–90 percent. Would this apply to them?

EL: Cincinnati Children's census is about 90 percent. That's the same as in Canada. In Canada, when we started working with the Ottawa Hospital on these issues, they reported their census in excess of 100 percent. If your average bed occupancy is 85 or 90 percent, then every peak in census hits the ceiling. Every peak means that emergency patients are going to be boarded, quality of care is diminished, and yet the next day's valley will result in waste. In short, hospitals lack capacity because of the way they choose to do business.

PV: What does it take to make this happen? Why isn't every place adopting this?

EL: That's a key question. The answer is multifactorial. First and foremost, if the hospital does not have an inspired and committed leadership, it's not going to happen. If the hospital CEO, personally, is not supportive of this intervention, it's not going to work. Second, surgeons do not realize that if they agree to smoothing, they would increase their volume, reduce their overtime, and improve their and patient satisfaction. At Cincinnati Children's, despite a one-third reduction in waiting time for emergent and urgent surgery, they increased the number of cases and yet the overtime dropped by 57 percent.

PV: I think the principle could be said, by a surgeon, that you don't cure constipation by adding more colon.

EL: Absolutely. Leadership and education are critical. Surgeons should be educated to appreciate the benefits of this intervention. The third reason is that in order to accomplish smoothing, hospitals should do pretty intense data analysis. Not all hospitals have these resources,

and the government should do its job to invest in hospitals getting the necessary technical support. Last but not least, I think emergency physicians must do a better job of explaining to the public the real cause of overcrowding and boarding. No matter what you do in your emergency department—and I am not suggesting that emergency departments are flawless—you alone cannot resolve overcrowding. That message should be known by the public.

PV: What would happen nationwide from implementing this intervention?

EL: The return on investment would be huge.

In 2012, two leading US health policy experts, Dr. Arnold Milstein and Dr. Stephen Shortell, in their piece "Innovations in Care Delivery to Slow Growth of US Health Spending" in the *Journal of the American Medical Association*, estimated that national diffusion of patient-flow optimization—optimally managing patient demand and health care capacity—has the potential to reduce total US per capita spending by 4 percent to 5 percent, which is \$120–\$150 billion a year. This intervention does not require capital investments. Quite the contrary, hospitals that implemented this approach saved millions of dollars and many human lives. ☺



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New ACEP Clinical Policy on Transient Ischemic Attack

BY BRUCE M. LO, MD, MBA, RDMS, FACEP



If non-contrast brain MRI is not readily available, it's reasonable for physicians to obtain a non-contrast head CT as part of the initial TIA workup to identify TIA mimics (eg, intracranial hemorrhage, mass lesion). However, non-contrast head CT should not be used to identify patients at high, short-term risk for stroke.

In June 2016, the ACEP Board of Directors approved a new clinical policy on the evaluation of adult patients with suspected transient ischemic attack (TIA), which was developed by ACEP's Clinical Policies Committee. This clinical policy can also be found on ACEP's website, and has been submitted for inclusion on the National Guideline Clearinghouse website.

TIA is part of a spectrum that involves ischemia of the central nervous system, with approximately 240,000 cases a year in the United States. Although most TIAs last less than one to two hours, by definition, "TIAs have a resolution of symptoms within 24 hours without evidence of an acute infarction on imaging. Since approximately 15 percent of all ischemic strokes are preceded by a TIA, timely evaluation for high-risk conditions, such as carotid stenosis and atrial fibrillation, is important.

Based on the feedback from the ACEP membership, the committee focused on four clinical questions about the evaluation of TIA in the emergency department. A systematic review of the evidence was conducted, and the committee made recommendations (A, B, or C) based on the strength of evidence (see Table 1). This clinical policy received input and comments from emergency physicians, neurologists, and members of the American Heart Association/American Stroke Association during the 60-day open-comment period. These responses were used to refine and enhance this clinical policy.

CRITICAL QUESTIONS AND RECOMMENDATIONS

QUESTION 1. In adult patients with suspected TIA, are there clinical decision rules that can identify patients at very low short-term risk for stroke who can be safely discharged from the emergency department?

Patient Management Recommendations

- **Level A:** None specified.
- **Level B:** In adult patients with suspected TIA, do not rely on current existing risk stratification instruments (eg, ABCD2 score) to identify TIA patients who can be safely discharged from the emergency department.
- **Level C:** None specified.

QUESTION 2. In adult patients with suspected TIA, what imaging can be safely delayed from the initial ED workup?

Patient Management Recommendations

- **Level A:** None specified.
- **Level B:** None specified.
- **Level C:** (1) The safety of delaying neuroimaging from the initial ED workup is unknown. If non-contrast brain MRI is not readily available, it's reasonable for physi-

Table 1. Translation of Classes of Evidence to Recommendation Levels

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

• LEVEL A RECOMMENDATIONS.

Generally accepted principles for patient care that reflect a high degree of clinical certainty (eg, based on evidence from one or more Class of Evidence I or multiple Class of Evidence II studies).

• LEVEL B RECOMMENDATIONS.

Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (eg, based on evidence from one or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

• LEVEL C RECOMMENDATIONS.

Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations were made, "consensus" is placed in parentheses at the end of the recommendation.

cians to obtain a non-contrast head CT as part of the initial TIA workup to identify TIA mimics (eg, intracranial hemorrhage, mass lesion). However, non-contrast head CT should not be used to identify patients at high, short-term risk for stroke. (2) When feasible, physicians should obtain MRI with diffusion-weighted imaging to identify patients at high short-term risk for stroke. (3) When feasible, physicians should obtain cervical vascular imaging (eg, carotid ultrasonography, CT angiography [CTA], or magnetic resonance angiography [MRA]) to identify patients at high short-term risk for stroke.

QUESTION 3. In adult patients with suspected TIA, is carotid ultrasonography as accurate as neck CTA or MRA in identifying severe carotid stenosis?

Patient Management Recommendations

- **Level A:** None specified.
- **Level B:** None specified.
- **Level C:** In adult patients with suspected TIA, carotid ultrasonography may be used to exclude severe carotid stenosis because it has an accuracy similar to that of MRA or CTA.

QUESTION 4. In adult patients with suspected TIA, can a rapid ED-based diagnostic protocol safely identify patients at short-term risk for stroke?

Patient Management Recommendations

- **Level A:** None specified.
- **Level B:** In adult patients with suspected TIA without high-risk conditions, a rapid ED-based diagnostic protocol may be used to evaluate patients at short-term risk for stroke. (High-risk conditions include abnormal initial head CT result [if obtained], suspected embolic source [presence of atrial fibrillation, cardiomyopathy, or valvulopathy], known carotid stenosis, previous large stroke, and crescendo TIA.)
- **Level C:** None specified.

Because of the high risk of stroke after a TIA, timely diagnostic testing for modifiable risk factors is important. This can be done in a number of ways, including an ED-based protocol (eg, ED observation) and should include neurovascular imaging.

While there are a number of risk stratification instruments for TIA, none are currently sufficient in identifying patients who are at low short-term risk for stroke and who can be safely discharged from the ED. More research is needed to develop better risk-stratification instruments as well as identifying which diagnostics tests should be performed during the ED visit versus as an outpatient. ☺

DR. LO is an associate professor of emergency medicine at Eastern Virginia Medical School, Norfolk, Virginia, and medical director of the department of emergency medicine at Sentara Norfolk General Hospital, Norfolk, Virginia.

THE WRONG DRUGS FOR A SUPERBUG

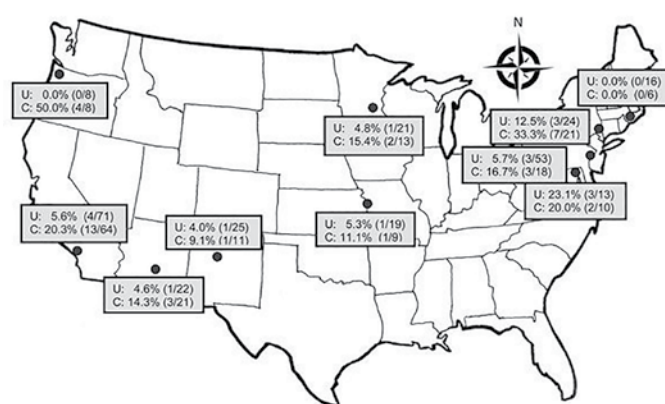
In the September 2016 edition of the Centers for Disease Control and Prevention (CDC) journal *Emerging Infectious Diseases*, my colleagues and I report on a 2013–2014 study of US emergency department patients presenting with acute pyelonephritis.¹ A multiple-antibiotic-resistant *E. coli* that produces extended-spectrum beta-lactamases, referred to as ESBL, was the cause of as many as 8 percent of uncomplicated pyelonephritis cases and 17 percent of complicated pyelonephritis cases in some locations (see Figures 1 and 2). The study was done by EMERGENCY ID NET, an emergency department–based sentinel research network for emerging infections funded by the CDC since 1995, and involved 10 geographically diverse large university-affiliated US departments.

Importantly, we found that about three-quarters of patients with acute pyelonephritis due to ESBLs were empirically treated with antibiotics *lacking* in vitro activity—in other words, they were treated with the wrong drugs. This is a big problem. Treatment antibiotic in vitro activity discordance is associated with bad outcomes.

THE FRQ/ESBL CONNECTION

While you may not have noticed the emergence of ESBLs, you probably have seen more and more of your culture results showing *E. coli* resistant to our go-to pyelo-

Figure 1.



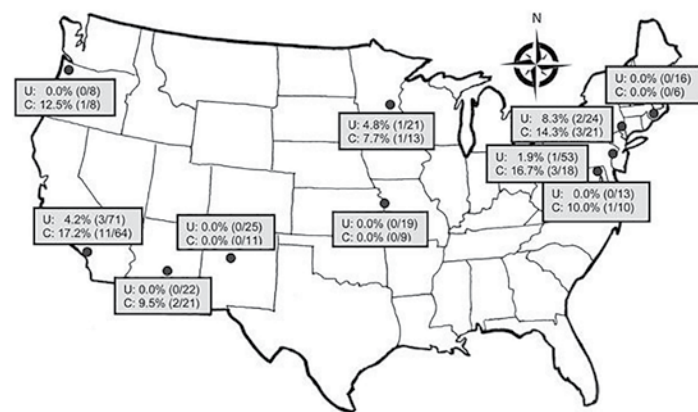
Prevalence of fluoroquinolone-resistant *Escherichia coli* infection among emergency department patients with uncomplicated (U) and complicated (C) pyelonephritis by study site, United States, July 2013–December 2014. In vitro resistance to ciprofloxacin and/or levofloxacin is shown as % (number of patients with a resistant isolate/total number of patients tested).

nephritis antibiotics, fluoroquinolones (eg, ciprofloxacin and levofloxacin). Compared to when we studied this about a decade ago, overall rates of fluoroquinolone-resistant infections (FQR) increased from 4 percent to 12 percent. However, in some locations and among some patients with resistance risk factors and high-risk infections (ie, complicated infections, males, structural/functional urological conditions, antibiotic use, health care exposure, international travel within 90 days, or prior FQR or ESBL infection), FQR rates

exceeded thresholds set by Infectious Diseases Society of America (IDSA) guidelines for which a different treatment strategy is recommended—FQR rates were above 10 percent and even 20 percent in some circumstances.²

At FQR rates of 10 to 20 percent, IDSA recommends a long-acting antibiotic of another class (eg, ceftriaxone or a single daily dose of an aminoglycoside) in addition to a fluoroquinolone. At FQR rates exceeding 20 percent, IDSA recommends abandoning fluoroquinolones, and this is where ESBLs come

Figure 2.



Prevalence of fluoroquinolone-resistant and ESBL-producing *Escherichia coli* infections among patients with uncomplicated and complicated pyelonephritis by study site, United States, July 2013–December 2014. Each dot indicates a study site; the line to show the general trend between fluoroquinolone resistance and ESBL-producing *E. coli* was generated by using simple linear regression.

into play. Risk factors for ESBL infections were the same as for FQR. However, about one-third of patients with ESBL infections had no risk factors, indicating that ESBLs are now endemic in some US communities. This is becoming much like the situation seen in South America, India, Southeast Asia, and Southern Europe.

Note, however, that high FQR rates and emerging ESBLs are not yet a problem everywhere in the United States—so watch for in-

CONTINUED on page 14

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creasing FQR rates. Your lab may or may not indicate an isolate is an ESBL strain. However, if it reports resistance to ceftriaxone, you can assume the bacteria are ESBL producers.

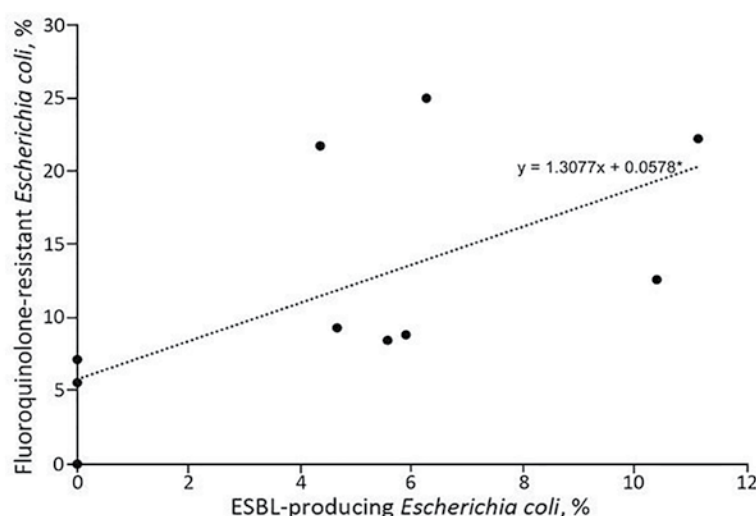
Locations with high FQR rates also have high ESBL rates (see Figure 3), so emergency physicians now need to know reliable empirical treatments for this emerged pathogen. ESBLs are resistant to *all* commonly used cephalosporins (eg, ceftriaxone) and frequently resistant to both fluoroquinolones and gentamicin. ESBLs are nearly universally susceptible to carbapenems, including long-acting ertapenem. The majority but not all isolates are susceptible to piperacillin-tazobactam and amikacin. Some newer but less available agents (ceftazidime-avibactam and ceftolozane-tazobactam) are very active against ESBLs.

CHOOSING THE RIGHT DRUGS

The real question is, when do I pull the ESBL antibiotic trigger? Here is what I think is the best answer:

In settings with high FQR rates (above 15 percent), where ESBL-producing *E. coli* infections have emerged, and among persons with antimicrobial drug resistance risk factors—and especially for patients with or at risk for severe sepsis—you should consider empirical treatment with a carbapenem or another agent found to be consistently active based on the local antibiogram. Checking a

Figure 3.



Prevalence of fluoroquinolone-resistant and ESBL-producing *Escherichia coli* infections among patients with uncomplicated and complicated pyelonephritis by study site, United States, July 2013–December 2014. Each dot indicates a study site; the line to show the general trend between fluoroquinolone resistance and ESBL-producing *E. coli* was generated by using simple linear regression.

patient's past infections and understanding local resistance rates are key. If you're lucky enough to have an ED pharmacist, having them track and report current resistance rates should be a priority. (You can expect updated IDSA guidelines soon.)

How about outpatient treatment? We've become good at treating-and-strengthening many patients with acute pyelonephritis. However,

at the present time, we have no oral antibiotics that are consistently active against ESBLs to treat an upper-tract (pyelonephritis) infection. This is where the superbug headlines have some justification.

If you endeavor to send a patient home and ESBLs are a concern, make sure to culture the urine, get the patient's phone number, and start out with an ertapenem dose before dis-

charge. Then there's no perfect choice for oral antibiotics. Combining a beta-lactamase inhibitor drug, amoxicillin-clavulanate, with a third-generation cephalosporin, like cefdinir, may allow the latter to evade beta-lactamase destruction.³ Alternatively, you can go with a fluoroquinolone and hope since these antibiotics, when active, have the best clinical performance. Then be sure to give good discharge instructions and check the culture result in two days when you can contact the patient and make adjustments based on the susceptibilities. ☛

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EM DOCS ON
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DR. MOODY, founder of the EM Docs Facebook group, is president of the Tennessee College of Emergency Physicians and former emergency department chair for Mountain States Health Alliance.

Facebook Group Discussions Support Physicians in Practice

EM Docs members discuss non-opioid headache treatments, sugar for penile edema, Haldol for vomiting, and ST elevation in aVR



by K. KAY MOODY, DO, MPH

Our virtual doctors' lounge, EM Docs, continues to grow! As of the writing of this column, there were 8,292 members—and we're growing daily, with 365 requests awaiting verification as members add their colleagues and word gets around about our camaraderie!

There was a time when physicians met in a physical lounge, sat together, chatted about patients and interesting cases, and lifted one another with encouragement both professionally and personally. With the pressures in our current health care system, we find ourselves stretched so thin that we barely have time to spend with our families, much less with time to support one another. Physicians are smart, and we've found a way to decrease the stresses by joining together virtually!

Again, in this EM Docs column, I'd like to share some of our most helpful conversations. To maintain the privacy of the group, there won't be personal attribution or details provided.

Non-Opiate Treatment of Headaches

As the saying goes, "everything old is new again." Intranasal lidocaine delivered with a mucosal atomizing device (MAD) is regaining popularity as we search for ways to avoid opiate use in the emergency department (see Figure 1). EM Docs shared both old and new articles for an evidence-based approach to headache treatment.

"Evaluation of Efficacy of Intra-Nasal Lidocaine for Headache Relief in Patients Refer to Emergency Department" is a double-blind, randomized controlled trial studying 90 adult patients with acute headache.¹ The dose was one puff of 10 percent lidocaine or normal saline per nostril. After intervention, the mean visual analog scale (VAS) scores were significantly lower in the lidocaine group than the placebo group at 1, 5, 15, and 30 minutes.

Since we lack 10 percent lidocaine in our departments, other (older) articles were referenced including "Intranasal Lidocaine for Treatment of Migraine: A Randomized, Double-Blind, Controlled Trial."² In this study, 81 patients with headache were given either a 4 percent solution of intranasal lidocaine or a saline placebo. Fifty-five percent of patients in the lidocaine group had at least a 50 percent reduction of headache compared with 21 percent in the placebo group.

Some EM Docs in the group who had tried this technique used 1 to 1.5 mL per nare with reported success for patients who had failed other treatments.

Recent neurology guidelines for first-step

headache treatment are ketorolac 30 mg IV push or 30 to 60 mg intramuscular plus metoclopramide 10 mg IV push over two minutes plus diphenhydramine 25 to 50 mg IV push. Opiates for headaches are *not* recommended. When EM Docs were asked about their uses of MADs, their responses included fentanyl, Narcan, Versed, lidocaine for headache, awake intubations and nasopharyngolaryngoscopy, lidocaine with epinephrine or tranexamic acid for epistaxis, and ketamine.

Use Sugar to Reduce Penile Edema

A case report was presented with a patient who arrived with an edematous penis secondary to a metal ring he had placed at the base of his penis. Other EM Docs helped by suggesting a well-documented, but not widely known, "trick of the trade" use of sugar for reduction of edema, similar to the use of sugar for rectal prolapse. Several articles were referenced including "Paraphimosis—Pour Some Sugar On Me."³ This article described the steps as follows: 1) Mix 50 mL of 50 percent dextrose solution with 2 percent lidocaine jelly, 2) place gauze into the solution, 3) place soaked gauze on the glans of the penis, 4) cover with condom or condom foley, 5) wait one hour, and 6) reduce the paraphimosis.

Another referenced article, "Paraphimosis Treatment & Management," describes this method: 1) Apply 2% lidocaine gel to the penile skin for a few minutes to an hour before penile manipulation to reduce pain, 2) wrap the penis in plastic and apply ice packs, 3) use compressive elastic dressings, and 4) apply direct circumferential manual compression.

Haldol for Vomiting

Many of the EM Docs discussed successfully relieving vomiting in patients with gastroparesis and cyclic vomiting with doses of Haldol, ranging from 2 to 5 mg IV. Some also add 25 to 50 mg of IV Benadryl. Approximately 50 EM Docs reported using Haldol for vomiting with success on multiple occasions.

"Haloperidol for Treatment of Cannabinoid Hyperemesis" reports a case of cannabinoid hyperemesis syndrome (CHS) and cyclical vomiting where the CHS improved significantly after treatment with haloperidol in the emergency department.⁵

The dose was one puff of 10 percent lidocaine or normal saline per nostril. After intervention, the mean visual analog scale scores were significantly lower in the lidocaine group than the placebo group at 1, 5, 15, and 30 minutes.

Pay Attention to aVR

The patient with the ECGs in Figure 2 presented talking, then became unresponsive with pulseless ventricular tachycardia, was cardioverted, woke up, and had the second ECG performed. He was sent for catheterization and had critical left main stenosis and severe three-vessel disease.

Dr. Smith's ECG Blog has an excellent discussion on the clinical significance of augmented vector right (aVR) elevation:⁶

"Ischemic ST elevation in aVR occurs in two broad categories: 1) in patients with recognized STEMI (due to coronary occlusion, usually of the LAD) and is associated with

higher mortality than in patients without STE in aVR and 2) in patients without ischemic ST elevation, in which case there is always diffuse ST depression of subendocardial ischemia (which can be due to supply-demand mismatch or due to ACS). If due to ACS, this STE in aVR is associated not only with acute LM insufficiency, but alternatively with 3 vessel disease, or with LAD insufficiency."

EM Docs continue to use crowdsourcing to improve patient care in real time as well as to prevent burnout by supporting one another with camaraderie. Emergency physicians can't always share their challenges with their non-physician family members. EM Docs allows for true understanding of the bedside challenges that are unique to our profession. ☺

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Figure 1. Many EM Docs are using intranasal lidocaine delivered with a mucosal atomizing device for headaches to avoid opiate use.

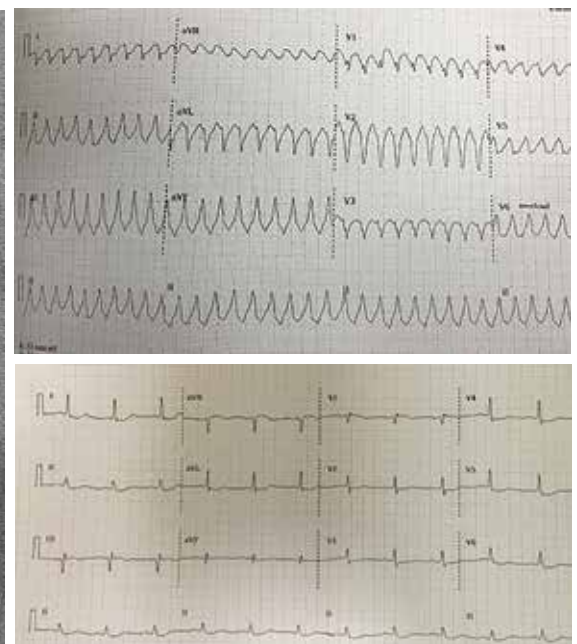


Figure 2. This patient's elevated aVR was associated with three-vessel disease.

ECG COURTESY OF TONY MACASSET, MD, EMERGENCY DEPARTMENT MEDICAL DIRECTOR AT VERNON MEMORIAL HEALTHCARE IN VEROONA, WISCONSIN.



Paying for Your Children's Education

Financial-aid planning for physicians and their college-bound children

by JAMES M. DAHLE, MD, FACEP

Q. *I have children who will soon be starting high school. What do I need to know about financial planning for college?*

A. There are a few key pieces of information emergency physicians need to know regarding paying for the college education of their children. The first is that by virtue of their high income, their family situation is likely to differ significantly from that of the average student. Average students and parents will fill out a Free Application for Federal Student Aid (FAFSA) or the similar College Scholarship Service (CSS) application and discover a difference between the parents' expected financial contribution (EFC) and the cost of attendance at their chosen school. That is not the case for the typical children of emergency physicians. What this means is that your children will not receive any need-based grants or scholarships, nor will they be able to take out federal and state student loans, at least as undergraduates, unless they are able to be considered independent from you (marriage, military service, or children). The children of many physicians will have to pay for school in a different manner than their parents did! It is still worth filling out the FAFSA just in case, especially if you will have multiple children attending expensive schools at the same time, but don't expect much. In addition, some schools require the FAFSA be filled out in order to receive merit-based scholarships.

Financial-aid planning is the process whereby some middle-class families may benefit from making the difference between the EFC and the college's cost of attendance as large as possible. This requires an understanding of what counts on the FAFSA (or CSS) and what doesn't. Then you transfer your assets from those categories that count (taxable investing accounts, savings accounts, 529s) to assets that do not (paying off debt, retirement accounts, life insurance). The theory is that this will allow students to get need-based grants and scholarships as well as to be eligible for loans. Most physicians will not benefit much from this process due to their high income. They will be much better off spending their time, effort, and money increasing their savings to help pay for college.

There are four pillars to successfully paying for children's education. Every situation is different, and it is likely that one or two of these pillars will be more important in your scenario than the others, but the larger the contribution from each of them, the easier the task will be.

The first pillar is school selection. Far too many parents together with their children choose a school without paying attention to the value received for the price paid. The cost of tuition and fees vary dramatically from one college to another, not to mention the cost of living of the city the school is located in and



the price of travel between your home and that city. There is also some variation in quality of education and peers at each school. But paying no attention whatsoever to the price tag is a huge mistake. High-school seniors have chosen their college for reasons as silly as, "I thought the houses in the town were pretty," or "The dorm rooms seemed nice," or "My friend is going there." In reality, if cost isn't one of the top three considerations in choosing a school, a mistake is likely to be made. This approach argues for attending a state university in your state most of the time. Exceptions can be made for inexpensive private colleges and, perhaps for a very bright child, one of the premier national private universities, assuming it can be afforded. An even less expensive option can be attending a community college for the first two years prior to transferring to a state university to get the final degree, but there is usually a significant drop in educational quality that comes with that approach, which will make a difference for some students depending on their educational and career plans.

The second pillar is the child's contribution. This includes merit-based scholarships for athletics, academics, musical ability, or anything else. It also includes the child's savings, part-time work during the school year, and full-time work in the summers. An 18-year-old is an adult and could be expected to work for pay, even if the student might need some guidance with regard to choosing a college! Many students have learned their spare time as high-school seniors is better spent

applying for hundreds of scholarships than working for \$8 an hour scooping ice cream. College is a busy time, but it is not so busy that students cannot work part-time. An education may be appreciated more when part of it is paid for by the student.

The third pillar is college savings. Hopefully, most physicians will be able to save something for their children's college in between the time they pay off their own student loans and the time children enroll. The federal and many state governments have offered to help via tax breaks. The two main types of accounts used are Coverdell Education Savings Accounts (ESAs) and 529 plans. ESAs are hampered by a low contribution limit (\$2,000 per year) and no state tax break. The 529s have higher contribution limits, currently \$14,000 per year for each spouse, and you can even "front-load" up to five years' worth. Each state offers a 529, and some are better than others. While most 529s are "savings" plans, which can be used at any school in any state, others are "prepaid tuition" plans. With prepaid tuition plans, if you do not attend a school in that state, you may not be able to transfer the full value of the 529 to an out-of-state school. For this reason, tread very carefully when choosing a prepaid tuition type 529 plan.

To make matters more complicated, some states offer a state tax deduction or credit for using their plan, some states offer a deduction or credit for using any plan, and other states offer no deduction or credit at all. When choosing a plan, first see if your state offers a tax break and, if so, whether it requires you to

use your state's 529. If so, use that plan first. If not, or if you have already maximized the state tax break, then choose one of the top plans in the country with good investment options such as those of Utah, New York, Nevada, or Ohio. The largest benefit of an ESA or 529 plan is that the money, once contributed, grows in the account and is withdrawn from the account tax-free, as long as it is spent on legitimate education. If the money ends up not being needed, the beneficiary can be changed to another family member, including yourself. Unneeded money can also be withdrawn penalty-free, although not tax-free, if the child gets enough scholarships to pay for school. The earlier you start saving for college, the more of the heavy lifting the portfolio can do, thanks to compound interest, and the less you will need to save.

The fourth pillar is your current earnings. This is the main reason the FAFSA or CSS calculates your EFC to be such a high number. Typical emergency physicians will discover that their EFC is something like one-third of their annual income plus 6 percent of their non-retirement investments. It is true that for most physician families, a significant portion of the college expense can be simply cash-flowed. Unfortunately, one of the main benefits of cash flowing at least some of the cost of college is that tax credits and deductions are phased out for many emergency physicians. The American Opportunity Tax Credit (\$2,500 per year) starts phasing out at an adjustable gross income of \$90,000 (\$180,000 for married filing jointly, or MFJ). The Lifetime Learning Credit (\$2,000 per year) phases out at \$65,000 (\$130,000 MFJ). The tuition and fees deduction (\$4,000 per year) phases out at \$80,000 (\$160,000 MFJ).

Notice that there is no pillar called debt. There is little reason for any student to have student loans when finishing a bachelor's degree, especially the child of a physician. Certainly there is no reason for the physician to take on additional debt such as Parent PLUS Loans or a home-equity line of credit to pay for school. If the cost cannot be covered with savings, the earnings of the child, and the earnings of the parent, consider choosing a less expensive school.

If you put it all together, college education for the children of a physician should not be a terrible financial stress. Consider a school with tuition and fees of \$21,000 per year and a cost of living of another \$15,000 per year, for a total cost of attendance of \$36,000 per year. The child should be able to make \$5,000 in the summer and another \$4,500 during the school year with relative ease. Perhaps there is also \$2,000 in scholarship money. If the parents also saved up \$50,000 prior to enrollment, an additional \$12,500 per year can be spent. That leaves just \$12,000 per year, or \$1,000 per month, to cash flow. That should be easily doable on a physician income. ☘

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End-Tidal Capnography Is Not Just a One-Trick Pony: Part 1

Use capnography for detecting DKA and monitoring COPD

Capnography offers an indirect method to detect metabolic acidosis. EtCO₂ measurements have been shown to closely estimate arterial partial pressure of carbon dioxide (pCO₂) in healthy patients and also in the presence of metabolic derangements such as acidosis.

by KATRINA D'AMORE, DO, MPH, JUSTIN MCNAMEE, DO, AND TERRANCE MCGOVERN, DO, MPH

End-tidal capnography has gained momentum over the years as a standard for monitoring patients undergoing procedural sedation in the emergency department, with a level B recommendation coming out of ACEP's clinical policy regarding procedural sedation in 2014.¹ It can identify hypoventilation earlier than other monitoring tools we have at our disposal in the emergency department, but its utility doesn't end there. It can quickly and efficiently answer clinical questions beyond that of sufficient ventilation. Are the chest compressions being performed on your cardiac arrest inadequate? Should you stop resuscitation efforts? Is your hyperglycemic diabetic in diabetic ketoacidosis (DKA)? Is that nasogastric tube in the stomach? End-tidal capnography can lend insight to these questions that emergency physicians encounter on a daily basis. End-tidal carbon dioxide (EtCO₂) sensibly correlates with the pathophysiology of those and many other disease processes and can help guide decision making on your next shift.

Understanding the Capnogram

The end-tidal capnogram is separated into four separate phases (see Figure 1). Phase 0 begins during the inhalation phase of the respiratory cycle and the capnogram drops precipitously from its peak level at the end of expiration. Once the patient begins to exhale (phase I), the initial expired air is predominantly dead space with little expired carbon dioxide (CO₂), but as the more densely concentrated CO₂ is expired, there is a sharp increase in the end-tidal waveform that represents phase II. The waveform then plateaus during phase III, with slight increases in the CO₂

concentration from alveolar air. The discrete end-tidal number we refer to is the value at the end of phase III, the very end of expiration prior to inhaling the next breath. Depending on the situation, the actual waveform of the capnogram and/or the end-tidal value at the end of exhalation may help us with more than just determining hypoventilation in patients undergoing procedural sedation in the emergency department. (See our September 2015 article, "How to Use End-tidal Capnography to Monitor Asthmatic Patients," at www.acepnow.com/article/how-to-use-end-tidal-capnography-to-monitor-asthmatic-patients for more information on using capnography and for a detailed review on using capnography to evaluate asthmatic patients.)

A New Breathalyzer for Detecting DKA?

It's nearing the end of your shift when you sign up for your last patient of the day. This fast-breathing diabetic had been sitting in Fast Track for a leg infection, and when the glucometer flashed "HIGH," he was moved to your higher-acuity area for more workup. You cringe as you picture the needle puncturing his wrist for an arterial blood gas (ABG) test and wonder whether you'll be breaking out that insulin drip. DKA is an endocrine emergency hallmarked by hyperglycemia, ketonemia, and metabolic acidosis. Ma et al demonstrated that knowledge of the arterial pH in suspected DKA added little to clinical gestalt and altered the emergency physician's management in only 2.5 percent of cases.² Do we even need to subject our patients to this test? Although the pH of the often less painful venous blood gas has been shown to be

comparable to that of an arterial blood gas, you wish you had an even quicker noninvasive screening tool.³

Capnography offers an indirect method to detect metabolic acidosis. EtCO₂ measurements have been shown to closely estimate arterial partial pressure of carbon dioxide (pCO₂) in healthy patients and also in the presence of metabolic derangements such as acidosis. Bou Chebl et al illustrated that lower pCO₂ values correspond to lower pH and bicarbonate val-

ues in hyperglycemic diabetic patients, which is in line with the known pathophysiology of acid-base disturbances.⁴ In more severe cases of underlying metabolic acidosis, one would expect an increase in compensatory tachypnea and, therefore, lower EtCO₂ readings. But how low buys you an insulin drip and a costly ICU bed? According to recent data (see Table 1) among patients with screening Accu-Cheks greater than 550 mg/dL, an EtCO₂ of 35 or greater virtually guarantees that the patient is not in DKA with a sensitivity of 100 percent.⁴ On the other hand, EtCO₂s of ≤21 and ≤26 are 100 percent and 96 percent specific for DKA, respectively.⁴ Among patients with a blood glucose (BG) >250 mg/dL, an EtCO₂ greater or less than 24.5 is both 90 percent sensitive and 90 percent specific for DKA.⁵ In a pediatric population with hyperglycemia, similar cut-off points were delineated: an EtCO₂ of >29 and ≥36 were 83 percent and 100 percent sensitive in ruling out DKA, respectively, while an EtCO₂ of <29 ruled in DKA 100 percent of the time.⁶

There is no current consensus regarding which EtCO₂ levels can be used consistently in practice to rule in or rule out metabolic acidosis, and therefore DKA, in the right clinical setting; however, utilizing end-tidal capnography in the evaluation of diabetic patients with suspected DKA is a quick and noninvasive method both to approximate the presence and severity of metabolic acidosis and to guide your initial treatment and the patient's ultimate disposition. While no formal consensus exists, a screening EtCO₂ of ≥36 in your next hyperglycemic diabetic patient can rule out ketoacidosis and spare your patient an invasive ABG test.

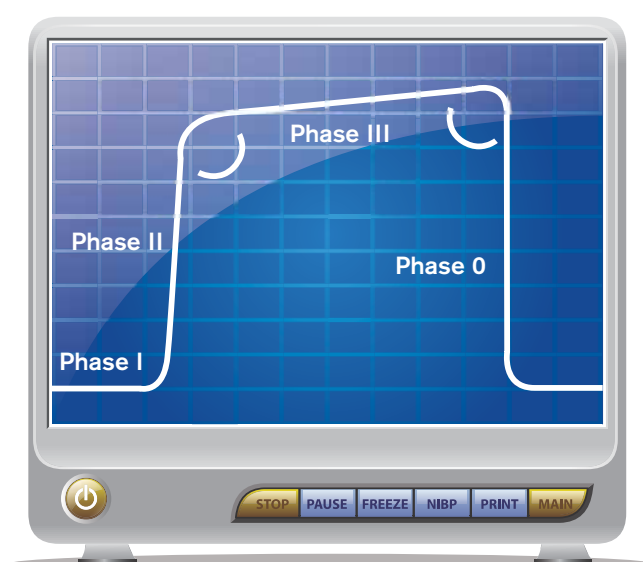
End-Tidal to Monitor COPD Exacerbations

People across the world continue to smoke despite the best efforts of the Truth campaign. COPD exacerbations seem as prominent as ever among ED visits and thus lead to difficult clinical decisions regarding treatment plans, intubation, and disposition. Many emergency physicians rely on ABG analysis in conjunction with their physical assessments to make the appropriate disposition for patients with COPD exacerbation. Could EtCO₂ also be the answer for COPD or just another far-fetched fairy tale?

Just like in most fairy tales, some things are just too good to be true. In a 2012 study, Soleimanpour et al were able to show a strong correlation between EtCO₂ and pCO₂ in normal healthy adults, with only a small discrepancy of 2 to 5 mmHg less in EtCO₂ as compared to

CONTINUED on page 18

Figure 1. Normal, healthy capnogram.



pCO₂ on ABG.⁸ In another study by Yosefy et al, EtCO₂ successfully predicted pCO₂ in emergency department patients in respiratory distress; however, these studies were conducted and proved a strong correlation between EtCO₂ and pCO₂ in “normal, healthy” patients.⁹ In additional studies of capnography use in respiratory patients, researchers have found the correlation between EtCO₂ and pCO₂ is not nearly as strong when the patient has shunting or mismatch perfusion as a result of underlying pulmonary disease. It is theorized that the increased dead-space ventilation creates an increasing gradient among EtCO₂ and pCO₂, therefore changing the correlation between one another to a mere moderate level. In a 2011 study by Kartal et al, the agreement between EtCO₂ and pCO₂ in COPD patients was a discrepancy of 8.4 mmHg less in EtCO₂ as compared to pCO₂.¹⁰ A similar study in COPD patients in 2015 was conducted by Taghizadieh et al and showed an even greater discrepancy among EtCO₂ and pCO₂, as much as 23 mmHg less in EtCO₂ compared to arterial pCO₂.¹¹ Based on these small clinical trials looking specifically at COPD patients, the EtCO₂ value is only minimally to moderately useful as a screening tool for hypercapneic respiratory failure. However, EtCO₂ seems to remain consistently below pCO₂ and may provide a starting point to monitor for improvement or worsening CO₂ retention. Unlike asthmatics, the numerical end value of

Table 1. Determining the Likelihood of DKA with Capnography

STUDY	POPULATION	ETCO ₂ LEVEL	SENSITIVITY	ETCO ₂ LEVEL	SPECIFICITY
Bou Chebl et al ⁴	Adults BG >550 mg/dL	≥35	100%	≤21	100%
				≤26	96%
Soleimanpour et al ⁵	Adults BG >250 mg/dL	>24.5	90%	<24.5	90%
Fearon et al ⁶	Children with hyperglycemia	>29	83%	<29	100%
		≥36	100%		
Gilhotra et al ⁷	Children	>30	100%		

the EtCO₂ capnogram can be used in your next COPD exacerbation patient to trend improvement or worsening respiratory failure, keeping in mind the correlation between EtCO₂ and pCO₂ is far from perfect in COPD patients. In the next "Tricks of the Trade" column, we'll review how to use end-tidal capnography to check orogastric/nasogastric tube placement and guide cardiopulmonary resuscitation. ☛

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First Look: 2015 EDBA Survey Results

This picture of emergency departments shows a spike in volume, structural changes, and boarding concerns

About 75 percent of departments with an annual visit volume of more than 40,000 reported a “fast track” for patient care, and about 35 percent had a clinical decision unit or observation unit.

by JAMES J. AUGUSTINE, MD, FACEP

The 2015 Emergency Department Benchmarking Alliance (EDBA) Performance Measures survey includes almost 1,200 emergency departments that served about 50 million patients, plus 57 additional freestanding emergency departments or urgent care centers.

The National Hospital Ambulatory Medical Care Survey (NHAMCS) from the Centers for Disease Control and Prevention (CDC) gives a statistical estimate of emergency department patients, treatment, and disposition based on federal demographic data and a statistical sampling of visits to American emergency departments. However, there has been no data release since December 2014, when the 2011 data tables were published. Emergency medicine leaders and ACEP have provided support for the CDC to publish this important release of data on an ongoing basis and have written to encourage them to publish data from years 2012 onward.

If we create an estimate based on the last published CDC numbers for 2011 of 136.3 million visits and include the historical average growth in emergency department visits since 1992 of about 2.5 percent over the subsequent five years, the American emergency department volumes seen in 2016 are likely going to hit about 150 million visits.

EDBA members reported that their volume increased as acuity remained stable. The ED patient volume at the same sites reporting in 2014 and 2015 increased by 4.3 percent—many departments had a higher increase in volume than that figure. Acuity mix, measured by physician level of service and by the percentage of patients who were admitted to the hospital

from the emergency department, remained stable from 2014 to 2015.

Children Versus Seniors

For 2015, there was a shrinking percentage of children treated in emergency departments, and therefore, the volume growth in American departments was based on increasing numbers of senior patients. This should be verified when the CDC publishes updated NHAMCS numbers, which will show an increasing level of Medicare patients.

There also was a growing number of trauma centers, particularly at the categories of Level II and Level III. Many of these new trauma centers serve injury populations that include large numbers of elderly patients. These service improvements are occurring in all regions of the country, not just the traditional Sun Belt locations.

Structure and Processing

Emergency departments have changed structure as they’ve grown in volume and complexity. Bed utilization was about 1,500 visits per patient care space. This was much lower in departments serving adult patient populations, at about 1,334 visits per care space. For departments serving pediatric patient populations, the figure was 1,887 visits per care space.

There also was an increased use of electronic information systems. Computerized physician order entry (CPOE) is present in more than 90 percent of emergency departments. That’s high enough that CPOE is now considered ubiquitous technology, and the EDBA survey question related to it will be removed from future data surveys.

Despite the increase in volume, the survey found that patient processing in emergency departments has improved. The door-to-doctor time was about 27 minutes on average, and the overall length of stay for all emergency patients was less than three hours. About 75 percent of departments with an annual visit volume of more than 40,000 reported a “fast track” for patient care, and about 35 percent had a clinical decision unit or observation unit. The percentage of patients who left the emergency department prior to the completion of treatment, however, increased to 2.4 percent.

Transfer/Inpatient Boarding

Patients who require transfer and inpatient boarding are a significant challenge to emergency department operations. The inpatient units were the site of disposition of emergency patients in about 16 percent of visits, and about 1.4 percent of patients were transferred

to another hospital, typically for admission. (The emergency department was the predominant front door for hospital admissions, with about 67 percent of hospital inpatients being processed through it.)

There was a stable volume of patient transfers: 1.4 percent of all patients, or almost 2 million a year. According to the 2011 CDC report, about one-third of patient transfers from emergency departments—or about 700,000 patients per year—were for mental health treatment.

The boarding time interval—the time from decision to admit until the patient physically leaves the emergency department—has stabilized for patients being placed in an inpatient unit of the hospital. The average boarding time in American departments was 111 minutes, but this time interval was very cohort-dependent. Emergency department inpatient boarding accounted for about 37 percent of the time an admitted patient spent in emergency. Boarding time ranged from about 170 minutes in departments with a patient volume of more than 80,000 to 67 minutes for departments seeing fewer than 20,000 patients. Emergency medicine leaders appear to have not been able to make much headway in reducing boarding time.

Emergency Medical Services

EMS continues to be an important source of volume for emergency departments, particularly for sicker patients. About 17 percent of patients arrived by EMS, and about 38 percent of those patients were admitted.

Diagnostic Testing

Diagnostic testing use is evolving in the emergency department. The survey found increased use of MRI scans and ultrasounds. MRI scans were performed a little more than 1 time per 100 patients seen, and ultrasound use was about 5.7 procedures per 100 patients seen. For the first time in the last 12 years, there was a leveling off of the utilization of ECGs, which were performed about 26 times per 100 patients seen. There was a continued downward drift in the use of CT scans, with a utilization rate of about 21 procedures per 100 patients.

Emergency physicians are responsible for high-quality and safe service in around 150 million patient encounters in the United States per year. Trends indicated in the NHAMCS database and in EDBA data surveys will continue to provide guidance regarding the value of emergency care in serving the needs of sicker, older, and more challenging patients. ☺





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Management Pearls and Pitfalls in Sickle Cell Disease

Many physicians undertreat sickle cell patients who do not appear in pain because they've learned to adapt to chronic discomfort

by ANTON HELMAN, MD, CCFP(EM), CAC, FCFP

Sickle cell disease (SCD) patients are at increased risk for a whole slew of life-threatening problems. One of the many reasons they are vulnerable is because people with SCD are functionally asplenic, so they're more likely to suffer from serious bacterial infections like meningitis, osteomyelitis, and septic arthritis. For a variety of reasons, they're also more likely than the general population to suffer from cholecystitis, priapism, leg ulcers, avascular necrosis of the hip, acute coronary syndromes, pulmonary embolism, and even sudden exertional death. Many of these diagnoses present with pain similar to a sickle cell crisis and can be challenging because the presentations of some are less typical than usual.

Sickle Cell Pain Crisis Is a Diagnosis of Exclusion

Patients with SCD can sometimes present a challenge when it comes to pain management because it's often difficult to discern whether they're malingering. The majority of SCD patients suffer real pain but may not look uncomfortable because they have learned to adapt to a lifetime of chronic pain. In the emergency department, they may appear calm, be preoccupied with their handheld device, or be casually chatting. The rates of true opioid addiction in sickle cell patients are low (less than 5 percent), and the literature suggests that emergency physicians undertreat pain in sickle cell patients. I recommend that unless there is clear evidence the patient does not have SCD, take the patient's complaint seriously and use analgesics aggressively in the emergency department.

As in all of emergency medicine, physicians need to think of the worst diagnoses first. Therefore, it is imperative not to assume that a patient with SCD who is in pain is suffering from a sickle cell crisis. If the pain is different from previous pain crises, broaden your differential diagnosis to include not only all the painful conditions that should be considered in all emergency patients but also sickle cell-specific conditions such as acute chest syndrome. The diagnosis of a pain crisis is a clinical one; no laboratory test will reliably determine whether the patient is suffering from a pain crisis, and SCD has been described in all races. Do not assume that a patient does not have SCD just because they have a light skin color. Sickle cell patients presenting with an uncomplicated pain crisis will often have normal vital signs. Any abnormal vital signs (especially fever) should raise the suspicion of alternative diagnoses. Examine joints and



soft tissues looking for evidence of cellulitis, septic joints, osteomyelitis, and joint avascular necrosis. Perform a careful respiratory exam looking for evidence of an acute chest syndrome. Look for hepatosplenomegaly if you have a concern for splenic sequestration. Lab tests are not routinely required for SCD patients presenting to the emergency department with a pain crisis. A complete blood count, reticulocyte count, liver function tests, bilirubin, lactate dehydrogenase, and electrolytes should be considered if you suspect another diagnosis, the patient is systemically unwell, or you suspect worsening anemia or jaundice. In SCD patients with fever, have a very low threshold to do a septic workup and start empiric antibiotics. An important pitfall in the diagnosis of a pain crisis is assuming that a normal serum hemoglobin rules it out. Patients with a higher baseline serum hemoglobin level are more likely to suffer pain episodes due to vaso-occlusion. Consider admission for febrile patients without an identified source. The reticulocyte count is of particular value in sickle cell patients who present with a sudden drop in their serum hemoglobin level in order to distinguish a sequestration crisis from an aplastic crisis.

Pain Management in the ED

Emergency physicians often underdose analgesics in SCD patients. A general rule of thumb for initial dosing of opioids is to administer the patient's usual total daily dose in a single IV dose. Frequent reassessments with self-reported pain should guide repeat doses. Consider hydromorphone or morphine every 15 to 30 minutes until pain is under control, and escalate the dose by 25 percent for uncontrolled pain. Consider adjunctive medications including acetaminophen, NSAIDs, and ketamine. Note that while NSAIDs have been shown to be effective in managing sickle cell pain crises, they should be avoided for long-term treatment of pain in SCD patients because of the potential renal side effects as these patients are at increased risk for chronic renal failure. Case reports support the effectiveness of ketamine as an opioid-sparing drug. While corticosteroids have been shown to reduce pain scores and length of stay, they are associated with high rates of pain recurrence, and so I do not recommend them.

Oxygen and Fluids: Do Not Give Routinely

Reserve supplemental oxygen for patients who are hypoxic. Oxygen has never been shown to improve outcomes in SCD patients suffering from a pain crisis. Supplemental oxygen is thought to suppress bone marrow and increase transfusion requirements. If the oxygen saturation is greater than 92 percent, no supplemental oxygen is needed.

Reserve fluid boluses for patients who are hypovolemic. While it is thought that dehydration may precipitate a pain crisis, overhydration does not help resolve a pain crisis and may have detrimental effects such as atelectasis, which may precipitate acute chest syndrome and hyperchloremic metabolic

acidosis, promoting sickling. Resuscitate hypovolemic patients only to euvolemia, and for maintenance fluids, use a hypotonic solution such as half normal saline (½ NS) or dextrose 5%–half normal saline (D5-½ NS).

Is There a Role for Red Blood Cell Transfusions?

There is no role for red cell transfusions in an uncomplicated acute pain crisis. Transfusions can lead to an increased risk of alloimmunization and may increase pain by increasing viscosity of blood leading to vaso-occlusion as well as precipitate acute chest syndrome and stroke.

Acute Chest Syndrome

Acute chest syndrome is the most common cause of death in SCD. Like all classic triads in medicine, the classic triad of acute chest syndrome (fever, hypoxia, and pulmonary infiltrate) is often not present. Acute chest syndrome can present fairly benignly with a bronchitis-like or pneumonia-like clinical picture with cough and shortness of breath, but patients often do not develop a fever. The pain of acute chest syndrome is characterized by a T-shirt distribution. A sickle cell patient with isolated chest pain without any other symptoms can be safely presumed to be suffering from a sickle pain crisis, whereas any associated respiratory symptoms should raise the possibility of acute chest syndrome. Any degree of hypoxia, even if the chest X-ray is initially normal, should be considered to be acute chest syndrome until proven otherwise. The sooner patients with acute chest syndrome are diagnosed, the sooner they can receive lifesaving treatment with a simple red blood cell transfusion or exchange transfusion in consultation with a hematologist. In addition to usual resuscitative measures, broad-spectrum antibiotics should be initiated.

Thanks to Dr. Richard Ward and Dr. John Foote, the guest experts on the EM Cases podcast that inspired this article. 📻

RESOURCES FOR FURTHER READING

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RESOURCE FROM EMERGENCY MEDICINE CASES WEBSITE

PODCAST: Episode 68 Emergency Management of Sickle Cell Disease (emergencymedicinecases.com/emergency-management-of-sickle-cell-disease). You can also add EM Cases to your podcast app via emergencymedicinecases.com/casting-setup.



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Playing Your PV Cards Right

Paucis Verbis cards provide a useful framework to demystify the differential diagnosis for petechiae and purpura



You simply have to know to assess the two questions when examining the patient during your encounter. Then you can pull out your PV card, and voilà, your afebrile well-appearing patient with palpable purpura very likely has autoimmune vasculitis.

by JEREMY SAMUEL FAUST, MD, MS, MA, AND LAUREN WESTAFER, DO, MPH

Most of the Free Open Access Medical Education (FOAM) that emergency physicians consume comes in forms that you wouldn't turn to during a shift. Podcasts and blogs are great, but they don't lend themselves well as on-the-fly references. However, there are some forms of FOAM that you can and should utilize during shifts, and on a recent episode of FOAMcast, we covered some of our favorites. Among the most widely used "just in time" resources for FOAM are the Paucis Verbis (PV) cards published by the blog Academic Life in Emergency Medicine.

Currently, there are more than 150 PV cards available in many forms, including individual PDFs that can be saved ad hoc on any device or, if you like to be more organized, in one of several apps in your phone or computer (Evernote, AgileMD, or even a Dropbox folder). We used to recommend saving lots of these on your personal device, but with the ubiquity of the Internet, sometimes we find it is easier to Google the cards when you need them. The topics covered in the PV card series include an impressive range, such as cardiology, hematology, toxicology, and many more.

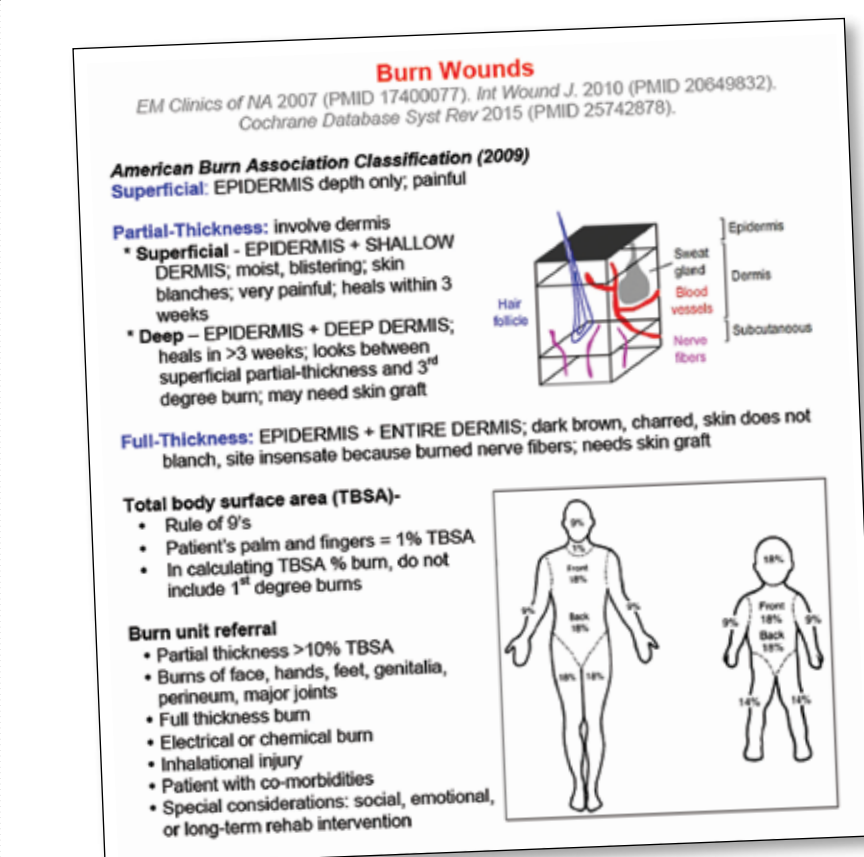
Among our most favorite PV cards of all time (yes, we have favorite PV cards; we are considering therapy) is "An Approach to Rashes." The card (actually it's three pages) is based on a popular article published in *The Journal of Emergency Medicine* from 2010 by Heather Murphy-Lavoie, MD, and Tracy Leigh LeGros, MD, PhD. The card has a succinct set of definitions of rash descriptors (nodule versus plaque, etc.) and some high-yield reminders (eg, the differential diagnosis of an acute rash co-presenting with hypotension, meningococemia, toxic shock syndrome, Rocky Mountain spotted fever, toxic epidermal necrolysis, and Stevens-Johnson). Most useful are the four flow charts that provide an excellent framework for rashes that are important to identify in the ED setting.

Undaunted by the fact that FOAMcast is an audio program with absolutely no visual component other than our companion website, FOAMcast.org, we decided to tackle one of the four charts and dedicate an entire show to it. We're almost positive we are the first people to have ever published an entire podcast about petechiae and purpura. Yeah, we're kind of proud that we pulled it off.

So if we could do a podcast about rashes without the help of visual aids, then why not try to do our column the same way? Well, here goes.

No Visual Needed

The dermatologists remind us that purpura is the umbrella term for purple discoloration



This card was updated by Dr. Christian Rose (UCSF-SFGH) to reflect current evidence that topical antibiotics and honey are IN, while silver sulfadiazine is OUT for partial-thickness burns.

of the skin due to extravasated blood. These lesions don't blanch. Petechiae are the small ones (less than 3 mm), while ecchymosis are the larger ones (greater than 5 mm.) With that in mind, the purpura flowchart only asks two questions: 1) Is the patient toxic/febrile? 2) Are the lesions palpable or non-palpable? This means that when it comes to purpura, there are only four conditions total: a toxic-appearing/febrile patient with either palpable (1) or non-palpable lesions (2) or a non-toxic-appearing/afebrile patient with either palpable (3) or non-palpable lesions (4). That's it. The best part is you really don't have to memorize the differential diagnosis of these four conditions. You simply have to know to assess the two questions when examining the patient during your encounter. Then you can pull out your PV card, and voilà, your afebrile well-appearing patient with palpable purpura very likely has autoimmune vasculitis.

We chose this particular example because the differential diagnosis for that branch of the decision tree conveniently has only one entry. What if that same patient had non-palpable purpura? The only possibility is idiopathic thrombocytopenic purpura (ITP). That means that if you have an overall well-appearing patient with non-blanching purple spots,

you know it's either autoimmune vasculitis or ITP. Now all you would need to do is touch the rash to decide which one it is. If you could feel the lesions, it would be ITP—not bad! The febrile/toxic branches have a few more options for the differential diagnosis, which is why you'll want to have the PV card handy. The card also has similarly useful flowcharts for maculopapular, erythematous, and vesiculobullous rashes. The major branch points in these decision trees focus, again, on the sick versus not-sick distinction, as well location and distribution of the lesions and the presence or absence of Nikolsky sign. With just those few questions in mind, you can easily delineate an impressive number of rashes.

For more PV cards, check out ALIEM.com, and as always, you can download our recent episodes at FOAMcast.org or on iTunes. In addition to our show on "just in time" FOAMed resources, we've recently recorded shows covering news on intracranial hemorrhage management (spoiler: aggressive blood pressure control seems to be unnecessary; also transfusing platelets for spontaneous intracranial hemorrhage might be a bad thing after all), an entire show on the pericardium, and a show covering the various types of altitude-associated illnesses. ☺



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Asthma & Intussusception

PO versus IV corticosteroids for asthma and recurrence rate of intussusception after reduction



by LANDON JONES, MD, AND RICHARD M. CANTOR, MD, FAAP, FACEP

The best questions often stem from the inquisitive learner. As educators, we love, and are always humbled by, those moments when we get to say, "I don't know." For some of these questions, you may already know the answers. For others, you may never have thought to ask the question. For all, questions, comments, concerns, and critiques are encouraged. Welcome to the Kids Korner.

Question 1: Are there differences in efficacy between PO and IV corticosteroids for acute moderate to severe asthma exacerbations in children?

In children, we're unable to find any studies that show a benefit of IV steroids over PO steroids for asthma exacerbations. There is a paucity of pediatric-specific studies, and like adult studies, there are differences in dosing and types of steroids. For instance, one study shows that 2 mg/kg of oral prednisolone (max dose 120 mg BID) demonstrates no significant benefit compared to 1 mg/kg IV methylprednisolone (max dose 60 mg four times daily) in regard to hospital length of stay (LOS).¹ These aren't the most common dosing regimens, and while LOS is important, it isn't an emergency department-specific outcome.

Barnett et al compared IV versus PO corticosteroids in 49 children with moderate to severe asthma exacerbations. The authors evaluated respiratory endpoints such as respiratory rate, oxygen saturations, and FEV1 exhalation volume as well as hospital admission rates. It was a randomized, double-blind, controlled trial comparing oral methylprednisolone (2 mg/kg) with IV methylprednisolone (2 mg/kg). In this study, there was no difference in hospital admissions between the two groups (48 percent PO versus 50 percent IV; $P=0.88$). All these patients had moderate to severe asthma exacerbations.²

As mentioned earlier, there's a paucity of pediatric data comparing PO versus IV corticosteroids for moderate to severe asthma exacerbations. That said, there is a 2001 systematic review and meta-analysis addressing early administration of corticosteroids for acute asthma exacerbations. Early administration of systemic corticosteroids, whether IV, IM, or oral, significantly decreased hospital admissions in patients with acute asthma exacerbations. These results included 11 total studies with both children and adults (pooled odds ratio, 0.40; 95% CI, 0.21–0.78).³ Early administration of systemic corticosteroids appears to be important—potentially more than the particular route of administration.

Summary: We can find no studies that demonstrate a significant clinical benefit of IV over PO corticosteroids in children with

moderate to severe asthma exacerbations. The data are very limited. However, there are studies that suggest early administration of systemic corticosteroids is important.

Question 2: In children, what's the recurrence rate of intussusception after enema reduction, and can they be safely discharged from the emergency department after observation?

To begin, a limitation in looking at this topic of disposition is that a prospective study is unlikely unless a multicenter study is developed; we're limited to retrospective data at this time.

A 2010 retrospective review by Whitehouse et al evaluated kids over a 12-year period (309 total children younger than or equal to 18 years of age) who had been diagnosed with intussusception. They admitted 261 (84.5 percent) and discharged 48 (15.5 percent) from the emergency department. During this period, 138 of 261 children were reduced by enema, and the rest (123/261) were reduced surgically. Recurrence after enema reduction occurred in 10 of 138 (7.2 percent) admitted patients and 4 of 48 (8.3 percent) discharged patients. Of the 14 children overall who had intussusception recurrences, six (42.8 percent) of the recurrences happened within 72 hours. The average LOS was 1.6 days; four of the recurrences happened within this time frame. The remainder of recurrences happened between 10 days and 21 months. There was no significant difference in delayed complications, defined as perforation or intestinal ischemia, between the discharged group and the admitted group.⁴ In terms of morbidity, the two groups appear similar.

In another, 10-year retrospective study with 568 total children at two tertiary care hospitals, 239 (42 percent) got emergency department "early discharge" where the average LOS was 7.2 hours, while 329 (58 percent) were admitted with an average LOS of 40 hours. The recurrence rate of intussusception was 8.8 percent (21/239) in the discharge group and 8.5 percent (28/329) in those admitted. There was a statistical difference in recurrences that were caught prior to discharge (20 of 28 in the admitted group versus 2 of 21 in the discharge group; $P=0.004$). There were no significant differences in morbidity between the discharge and admitted groups.⁵

A 2014 meta-analysis by Gray et al included 69 studies (15,163 total patients) in children. Overall, the recurrence rate of intussusception after enema reduction, whether contrast, ultrasound-guided, or air-contrast, was 12.7 percent (95% CI, 11.1%–

14.4%). The recurrence rate within 24 hours was 3.9 percent (95% CI, 1.5%–10.1%); within 48 hours, it was 5.4 percent (95% CI, 3.7%–7.8%). The authors argue that "the vast majority of recurrences will not be identified by overnight hospitalization."⁶

Conversely, a more recent 26-year retrospective study including 464 total children by Lessenich et al found a similar recurrence rate (5.6 percent) while noting that 18.5 percent of children required some form of hospital-level intervention defined as imaging/interventions for recurrence or suspected recurrence, or administration of parenteral narcotics or antiemetics.⁷

Summary: Intussusception recurrence rate after enema reduction, overall, appears to be about 5 to 12 percent. The majority of these recurrences don't present within the first 24 to 48 hours. It might be reasonable under certain instances (eg, good follow-up, reasonable distance from home, etc.) to discharge these children from the emergency department after a successful enema reduction and appropriate symptom-free observation period. Practitioners should at least recognize that this may be a change in practice when discussing these cases with our surgical colleagues. ➕

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Editor's Note: Cutting through the red tape to make certain that you get paid for every dollar you earn has become more difficult than ever, particularly in our current climate of health care reform and ICD-10 transition. The ACEP Coding and Nomenclature Committee has partnered with ACEP Now to provide you with practical, impactful tips to help you navigate through this coding and reimbursement maze.

Size Does Matter! But So Does Location and Complexity

by HAMILTON LEMPERT, MD, FACEP, CEDC

Question: What do I need to document for lacerations?

Answer: Three things are important to document for lacerations. First is the anatomical location (eg, left ring finger, right arm, face, neck, etc.). Different codes are used for

different parts of the body and, consequently, different payment amounts. Second, the size of the repaired laceration determines the code. The ranges are 2.5 cm or less, 2.6 cm–5.0 cm, 5.1 cm–7.5 cm, 7.6 cm–12.5 cm, 12.5 cm–20.0 cm, 20.1 cm–30 cm, and more than 30 cm. It is always best to list the actual measured length of the wound after closure. Third, the complexity of the repair also determines the code (eg, simple, intermediate, complex). Complexity is determined by how extensive the cleaning or debridement was, if it was a layered closure, if it was undermined, or if a drain was required. Lastly, it is important to document if you used a wound adhesive to repair the laceration. Visit www.acep.org/reimbursement for more coding and reimbursement information.

Brought to you by the ACEP Coding and Nomenclature Committee. ☺

DR. LEMPERT is chief medical officer, coding policy, at TeamHealth, based in Knoxville, Tennessee.

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Citrus Park ER (Tampa Bay)
Medical Center of Trinity (Tampa Bay)
Northside Hospital (Tampa Bay)
Palm Harbor ER (Tampa Bay)
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KANSAS

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Centerpoint Medical Center (Kansas City)
Lafayette Regional Health Center (Lexington)
Western Missouri Medical Center (Warrenburg)

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Parkland Medical Center (Derry)
Parkland Urgent Care Center (Salem)

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CHRISTUS Hospital - St. Elizabeth Minor Care (Beaumont)
CHRISTUS Spohn Hospital - Memorial (Corpus Christi)
CHRISTUS Spohn Hospital - Shoreline (Corpus Christi)
Bayshore Regional Medical Center (Houston area)
Clear Lake Regional Medical Center (Houston)
East Houston Regional Medical Center (Houston)
CHRISTUS Jasper Memorial Hospital (Jasper)
CHRISTUS Spohn Hospital - Kleberg (Kingsville)

Kingwood Medical Center (Kingwood)
Pearland Medical Center (Pearland)
CHRISTUS Hospital - St. Mary (Port Arthur)
CHRISTUS Santa Rosa Medical Center (San Antonio)
CHRISTUS Santa Rosa Hospital - Westover Hills (San Antonio)
CHRISTUS Alon/Creekside FSED (San Antonio)
CHRISTUS Santa Rosa - Alamo Heights (San Antonio)
Metropolitan Methodist (San Antonio)
Northeast Methodist (San Antonio)

TENNESSEE

Horizon Medical Center (Dickson)
ParkRidge Medical Center (Chattanooga)
Sequatchie Valley Emergency (Dunlap)
Hendersonville Medical Center (Hendersonville)
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Tennova Hospital - Lebanon (Lebanon)
Centennial Medical Center (Nashville)
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SKEPTICS' GUIDE TO EMERGENCY MEDICINE



DR. MILNE is chief of emergency medicine and chief of staff at South Huron Hospital, Ontario, Canada. He is on the Best Evidence in Emergency Medicine faculty and is creator of the knowledge translation project the Skeptics' Guide to Emergency Medicine (www.TheSGEM.com).

Amiodarone, Lidocaine, or Placebo in OHCA?

Comparing survival rates of each treatment

by KEN MILNE, MD

CASE: A 63-year-old man has an unwitnessed cardiac arrest. EMS arrives to find him in ventricular fibrillation. They quickly begin resuscitation efforts, including defibrillation that does terminate the dysrhythmia. They give amiodarone as part of their protocol but wonder if it will make a meaningful difference.

CLINICAL QUESTION: Are adult out-of-hospital cardiac arrest (OHCA) patients with refractory ventricular fibrillation or pulseless ventricular tachycardia who receive amiodarone or lidocaine more likely to survive to hospital discharge with good neurologic outcome?

BACKGROUND: Both lidocaine and amiodarone may be considered for the treatment of ventricular fibrillation or pulseless ventricular tachycardia that is unresponsive to defibrillation.¹

There are two randomized control trials demonstrating that the use of amiodarone led to more patients with a return of spontaneous circulation at the time of hospital arrival when compared to lidocaine or placebo.^{2,3}

In adult OHCA patients with refractory ventricular fibrillation or pulseless ventricular tachycardia, amiodarone or lidocaine is unlikely to provide a clinically important benefit.

cebo.^{2,3} However, these early benefits did not translate into a benefit in survival to hospital discharge or neurologically intact survival.

REFERENCE: Kudenchuk RJ, Brown SP, Daya M, et al. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med*. 2016;374(18):1711-1722.

• **Population:** Adult patients with nontraumatic OHCA and shock-refractory ventricular fibrillation or pulseless ventricular tachycardia after one or more shocks any-time during resuscitation.

—**Exclusions:** Patients who had already received open-label intravenous lidocaine or amiodarone during resuscitation or had known hypersensitivity to these drugs.

• **Intervention:** Rapid bolus of amiodarone or lidocaine.

• **Comparison:** Placebo.

• **Outcome:**
—**Primary:** Survival to hospital discharge.
—**Secondary:** Favorable neurologic function at discharge (modified Rankin Scale of 3 or less).

AUTHORS' CONCLUSIONS: Overall, neither amiodarone nor lidocaine resulted in a significantly higher rate of survival or favorable neurologic outcome than the rate with placebo among patients with OHCA due to initial shock-refractory ventricular fibrillation or pulseless ventricular tachycardia.

CONTINUED on page 31

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KEY RESULTS: There were 7,051/37,889 (18.6 percent) of patients with nontraumatic OHCA that had shock-refractory ventricular fibrillation or pulseless ventricular tachycardia. The intention-to-treat population consisted of 4,653 patients, and the per-protocol population consisted of 3,026 patients.

There was no statistical difference in the primary outcome of survival to hospital (amiodarone 24.4 percent, lidocaine 23.7 percent, and placebo 21.0 percent).

- Absolute difference: amiodarone versus placebo 3.2 percent (95 percent CI, -0.4 to 7.0; *P*=0.08)
- Absolute difference: lidocaine versus placebo 2.6 percent (95 percent CI, -1.0 to 6.3; *P*=0.16)

There was also no statistical difference in the secondary outcome of favorable neurologic function at discharge (amiodarone 18.8 percent, lidocaine 17.5 percent, and placebo 16.6 percent).

EBM COMMENTARY:

1) Statistical versus clinical significance: The study authors did not demonstrate a statistical difference in their primary outcome. However, there is a difference between statistical significance and clinical significance. The observed approximately 3 percent difference in survival to hospital discharge with treatment, if true, would translate into 1,800 lives saved yearly in North America for OHCA. They would have needed to enroll about 9,000 patients to establish if the 3 percent difference was statistically significant.

2) Intention-to-treat versus per-protocol analysis: The primary endpoint of this study was based on a per-protocol analysis of the cohort, which can introduce bias and make the treatment look better. They excluded 1,627 patients for a number of reasons. When they did an intention-to-treat analysis, the trend toward improvement became even less.

- Survival to hospital discharge: amiodarone 19 percent, lidocaine 18.4 percent, and placebo 17.6 percent
- Favorable neurologic function at discharge: amiodarone 14.4 percent, lidocaine 13.5 percent, and placebo 13.8 percent

3) Subgroup analysis: There were statistical differences observed in some prespecified subgroups. These should be viewed with caution and considered observational by nature. It is also important to remember that subgroup analysis can easily be misleading because the risk of type 1 error (incorrect rejection of a true null hypothesis) increases as the investigator makes more observations.

BOTTOM LINE: In adult OHCA patients with refractory ventricular fibrillation or pulseless ventricular tachycardia, amiodarone or lidocaine is unlikely to provide a clinically important benefit.

CASE RESOLUTION: The patient has a return of spontaneous circulation but does not survive to hospital discharge.

Thank you to Dr. Rory Spiegel from EM Nerd for his help with this review. Dr. Spiegel is a clinical

instructor at the University of Maryland and a recent graduate of Stony Brook’s resuscitation fellowship.

Remember to be skeptical of anything you learn, even if you heard it on the Skeptics’ Guide to Emergency Medicine. 🎧

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2. Kudenchuk PJ, Cobb LA, Copass MK, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med*. 1999;341(12):871-878.

3. Dorian P, Cass D, Schwartz B, et al. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med*. 2002;346(12):884-890.

ADDITIONAL RESOURCES

- **Podcast SGEM#162: Not Stayin’ Alive More Often with Amiodarone or Lidocaine in OHCA.** The Skeptics’ Guide to EM website. Available at: <http://thesgem.com/2016/10/sgem162-not-stayin-alive-more-often-with-amiodarone-or-lidocaine-in-ohca/>
- **The Case of the Perfect Imperfection.** EM Nerd website. Available at: <http://emcrit.org/emnerd/case-perfect-imperfection/>
- **ALPS: Amiodarone, Lidocaine or Placebo Study in OHCA.** REBEL EM website. Available at: <http://rebelem.com/alps/>

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To report SUSPECTED ADVERSE REACTIONS, call 1-844-273-2327 or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS
Live attenuated influenza vaccine (LAIV), intranasal: Avoid use of LAIV within 2 weeks before or 48 hours after administration of RAPIVAB, unless medically indicated.

- USE IN SPECIFIC POPULATIONS**
- Pregnancy: Use if benefit outweighs risk.
 - Nursing mothers: Caution should be exercised when administered to a nursing woman.

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Seqirus USA Inc.
King of Prussia, Pennsylvania 19406

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For flu patients in the emergency department who may not be appropriate for oral treatment^{1,2}

It only takes
one dose
to be

done

treating the flu with
Rapivab® (peramivir)¹

The first and only full course of antiviral flu therapy in a single dose^{1,2}

- Only one 15- to 30-minute IV infusion required
- Treats acute uncomplicated influenza in patients 18+ who have been symptomatic for no more than 2 days
- Appropriate for many patients, including those who cannot tolerate or may be noncompliant with oral flu treatment and those requiring IV hydration
- Can be used with OTC supportive therapies

Rapivab®
peramivir injection

One dose. Done.

Go to www.rapivab.com to learn more and view full Prescribing Information.

Important Safety Information

Rapivab® (peramivir injection) is indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days.

- Efficacy of Rapivab was based on clinical trials in which the predominant influenza virus type was influenza A; a limited number of subjects infected with influenza B virus were enrolled.
- Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Rapivab.
- Efficacy could not be established in patients with serious influenza requiring hospitalization.

Contraindications

Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to peramivir or any component of the product. Severe allergic reactions have included anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome.

Warnings and Precautions

- Rare cases of serious skin reactions, including erythema multiforme, have been reported with Rapivab in clinical studies and in postmarketing experience. Cases of anaphylaxis and Stevens-Johnson syndrome have been reported in postmarketing experience with Rapivab. Discontinue Rapivab and institute appropriate treatment if anaphylaxis or a serious skin reaction occurs or is suspected. The use of Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to Rapivab.

- Patients with influenza may be at an increased risk of hallucinations, delirium, and abnormal behavior early in their illness. There have been postmarketing reports (from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who were receiving neuraminidase inhibitors, including Rapivab. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made, but they appear to be uncommon. These events were reported primarily among pediatric patients. The contribution of Rapivab to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior.
- Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. Rapivab has not been shown to prevent such complications.

Adverse Reactions

The most common adverse reaction was diarrhea (8% Rapivab vs 7% placebo).

Lab abnormalities (incidence $\geq 2\%$) occurring more commonly with Rapivab than placebo were elevated ALT 2.5 times the upper limit of normal (3% vs 2%), elevated serum glucose greater than 160 mg/dL (5% vs 3%), elevated CPK at least 6 times the upper limit of normal (4% vs 2%) and neutrophils less than $1.0 \times 10^9/L$ (8% vs 6%).

Concurrent use with Live Attenuated Influenza Vaccine

Antiviral drugs may inhibit viral replication of a live attenuated influenza vaccine (LAIV). The concurrent use of Rapivab with LAIV intranasal has not been evaluated. Because of the potential for interference between these two products, avoid use of Rapivab within 2 weeks after or 48 hours before administration of LAIV unless medically indicated.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

References: 1. Rapivab [package insert]. Durham, NC: BioCryst Pharmaceuticals, Inc; 2014. 2. Kohno S, Kida H, Mizuguchi M, Shimada J; S-021812 Clinical Study Group. Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection. *Antimicrob Agents Chemother*. 2010;54(11):4568-4574. doi:10.1128/AAC.00474-10.

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