DR. JOHN LUMPKIN
A Pioneer of EM
SEE PAGE 11

KIDS KORNER
IV Fluids for Lumbar Puncture & Powerful Probiotics?
SEE PAGE 19

MYTHS IN EM
NSAIDs & the Anti-inflammatory Myth
SEE PAGE 23

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PLUS

SKEPTICS' GUIDE

DOACs FOR CANCER-RELATED VTE

SEE PAGE 18

BEDSIDE EDUCATION

ATRIAL FIBRILLATION AT CLUB VENTRICLE

SEE PAGE 13

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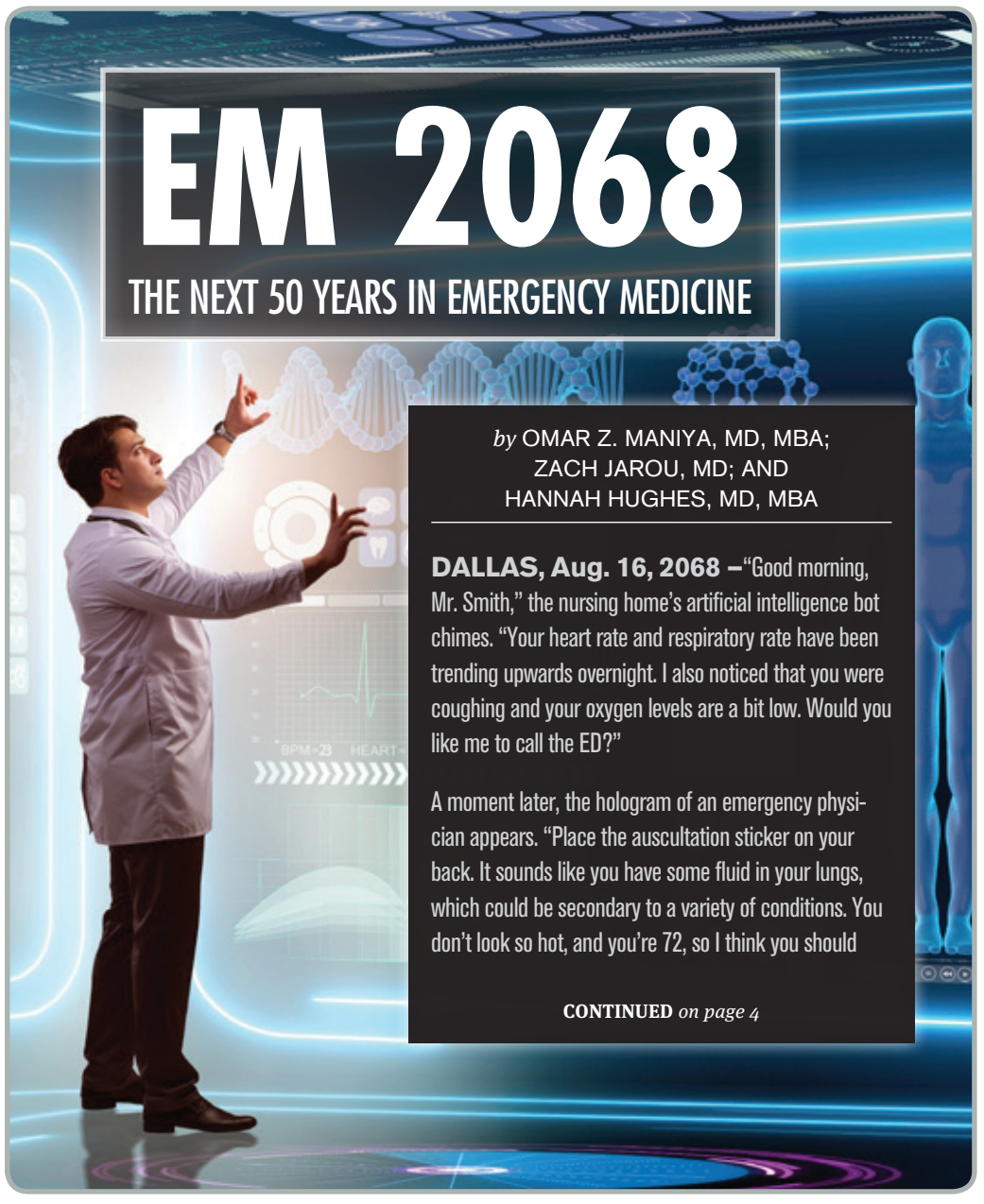

PHOTO: SHUTTERSTOCK.COM

by OMAR Z. MANIYA, MD, MBA; ZACH JAROU, MD; AND HANNAH HUGHES, MD, MBA

DALLAS, Aug. 16, 2068 –"Good morning, Mr. Smith," the nursing home's artificial intelligence bot chimes. "Your heart rate and respiratory rate have been trending upwards overnight. I also noticed that you were coughing and your oxygen levels are a bit low. Would you like me to call the ED?"

A moment later, the hologram of an emergency physician appears. "Place the auscultation sticker on your back. It sounds like you have some fluid in your lungs, which could be secondary to a variety of conditions. You don't look so hot, and you're 72, so I think you should

CONTINUED *on page 4*

WELLNESS

THE TOLL OF CARING FOR MEDICAL EMERGENCIES

We must start paying attention to PTSD in emergency medicine

by MEETA SHAH, MD

I cried at work the other day. It's not that crying in reference to a sad case is new to me; it's just new for the person who I am now.

A young woman rolled into my emergency department, trying to bleed to death; there was so much blood. Immediately my team flooded her room. Adrenaline took over, leaving no time for me to think or process or feel anything about the case. For what seemed like an eternity, I stood by her bedside, ignoring every other patient in the department. I did what any one of us would do: bark orders, call the blood bank, and run around with my team to do everything we can to resuscitate her. I stroked her hair as she cried. I stood by her husband as he was paralyzed in fear, all while watching her monitor with my heart racing.

We resuscitated her for over an hour before she was finally stable enough for the operating room. Finally, the chaplain was able to enter the room. He held hands with the patient and her husband and prayed with them while they cried.

Out of nowhere, I was suddenly triggered. I flashed back to a scenario many years ago, where a chaplain sat with me as I cried in a hospital. Every emotion from that day rushed at me in a matter of seconds. I turned on my heel, left the patient's side abruptly, and fled the room. My nurses were startled by my quick and dramatic departure. Before I could stop it, I found myself crying, vulnerable in front of my staff. I walked quickly, trying so hard to keep my tears hidden and avoid embarrassment. After years in practice, I finally felt like a leader in my department. I couldn't help but feel

CONTINUED *on page 22*

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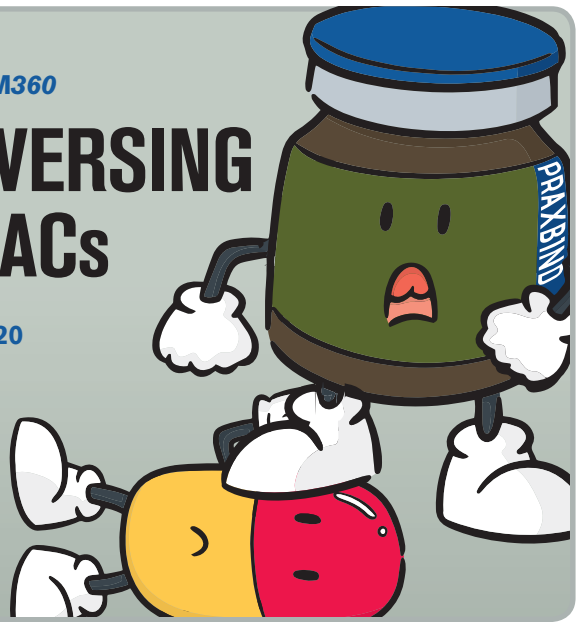

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THE BREAK ROOM

SEND YOUR THOUGHTS AND COMMENTS TO ACEPNOW@ACEP.ORG

It is rare for an article to inspire a letter to the editor; however, after reading "More Than Just 'I Do'" in the October issue of *ACEP Now*, I realized that sending you a note was more important than an extra 10 minutes of sleep.

I have always felt the professional support of ACEP—issues ranging from burnout to balance billing. However, I wish to thank you and your editorial staff for including an article touching on the unique challenges facing the LGBT physician community. I realize that we are a distinct minority among the ranks of our specialty. In fact, I've only met two other "out" LGBT ED physicians. Knowing that ACEP acknowledges these challenges and values our experience to the point of placing an inspirational article on the cover page of our monthly magazine nearly brought tears to my eyes.

Thank you for supporting our community and making me feel even more like I belong to our EM tribe.

Douglas P. Brosnan, JD, MD, FACEP
Roseville, California

NEWS FROM THE COLLEGE

UPDATES AND ALERTS FROM ACEP

Reimbursement Leadership Development Program Participants Chosen

More than 70 candidates from 22 ACEP state chapters applied for the ACEP Reimbursement Leadership Development Program (RLDP), which is designed to identify and train future leaders in emergency medicine reimbursement. ACEP will fund chosen applicants to travel to the ACEP Reimbursement and Coding conferences, the Leadership & Advocacy Conference, the Emergency Department Practice Management Association's Solutions Summit, ACEP headquarters structured sessions, and possibly an American Medical Association (AMA) CPT and Specialty Society Relative Value Scale Update Committee (RUC) meeting.

The inaugural RLDP class will include:

- B. Bryan Graham, DO
- Steven Kailes, MD, MPH, FACEP, FAAEM
- Lisa Maurer, MD, FACEP
- Archana Shah, MD, MBA
- James Shoemaker Jr., MD, FACEP

ACGME to Reconsider Common Program Requirements

The Accreditation Council for Graduate Medical Education (ACGME) recently released proposed changes to its Common Program Requirements (CPR) that threatened to remove the requirement for residencies to protect a portion of faculty time for core faculty. ACEP sent a letter to ACGME explaining why the proposed changes, a standardized, one-size-fits-all approach for all specialties, would be detrimental to emergency medicine. In response to letters from ACEP and other emergency medicine organizations, the ACGME has decided to reconsider its proposed changes.

ACEP Opposes Proposed Rule Regarding Immigrants, Medicare, and Medicaid

ACEP responded to a proposed rule issued by the Department of Homeland Security (DHS) that would implement new restrictions for some legal immigrants to obtain green cards if they have previously used public benefits such as food stamps, public housing, Medicare Part D low-income subsidies, or nonemergency Medicaid. In line with the public statement ACEP released immediately following the announcement of the rule, ACEP asked DHS to rescind the rule. ACEP believes that if finalized, the rule would cause fear and confusion, causing millions of Americans to disenroll from essential programs and stop receiving benefits for which they are eligible. The loss of Medicaid coverage, especially, would result in poorer health and health outcomes for affected individuals. It also could drive up ED use, uncompensated care costs, maternal and infant health risks, and transmission of infectious diseases.

ACEP Meets with SAMSHA About Suicide Hotline

Sandy Schneider, MD, FACEP, ACEP's associate executive director for practice, policy, and academic lines of service, met with the Substance Abuse and Mental Health Services Administration (SAMHSA) to discuss an enhanced national suicide hotline and a national phone number, such as 611.

ACEP responded to a request for comments from the Federal Communications Commission (FCC) related to the National Suicide Hotline Improvement Act of 2018. This act requires the FCC to conduct a study that examines the feasibility of designating a simple, easy-to-remember three-digit dialing code (such as an N11 code) that would be used for a national suicide prevention and mental health crisis hotline system. ACEP supports the creation of a new three-digit dialing code for mental health emergencies, as it would improve access to appropriate care and could reduce the prevalence of psychiatric boarding. However, ACEP believes that in addition to the new number, there must be adequate resources and services in the community that can provide feasible and safe alternatives to patients seeking care in the emergency department.

ACEP Meets with MedPAC About ED Coding and Documentation

On Dec. 13, 2018, ACEP met with key staff of the Medicare Payment Advisory Commission (MedPAC), an independent body created by Congress to advise legislators on Medicare payment and access issues. The goal was to educate their staff on trends in ED utilization and documentation and coding for ED visits.

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KEYNOTE SPEAKER

Corey Slovis, MD

Medical Director, Vanderbilt University Emergency Department
2018 Recipient, ACEP Outstanding Contribution in Education Award

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EM 2068 | CONTINUED FROM PAGE 1

come in for a 3-D ultrasound and possibly some IV antibiotics."

Emergency medicine has come a long way since ACEP was founded in 1968, from the first training program at the University of Cincinnati in 1970 to the founding of the Emergency Medicine Residents' Association (EMRA) in 1974 to finally being recognized as the 23rd medical specialty by the American Board of Medical Specialties (ABMS) in 1979. Fifty years later, TV shows like "M*A*S*H" and "ER" have been produced, EMTALA and the prudent layperson standard have been enacted, and more than 140 million patients seek care from us annually.

Our nation has gone from dermatologists treating our sickest and most vulnerable patients in emergency rooms to specialist emergency physicians providing care in sophisticated departments. We've transformed America's acute care system. However, as the residents who lead EMRA, it's our job to imagine and prepare for the future. Fifty years from now, emergency medicine will be as different from today's specialty as we are currently from our 1968 roots.

PHOTO: SHUTTERSTOCK.COM

By the time Mr. Smith arrives at his local freestanding emergency department, his vitals have been uploaded by EMS, he has been preregistered, and his copay has been automatically deducted from his virtual wallet. He skips the waiting room, and the Internet of Health Care Things–enabled ultrasound rolls itself to his stretcher. The operational software has used his transport time to preschedule an appointment with the ED ultrasound technician. Twenty minutes later, Dr. Casillas, his board-certified emergency physician, sits down on Mr. Smith's bed and holds his hand as she delivers the difficult news of a new lung mass and likely malignant effusion. At the same time, a virtual natural language processing scribe documents their conversation, codes the encounter, submits it to a national clearinghouse for reimbursement, and prompts her to place orders that had been previously placed for patients with similar presentations.

Dr. Casillas is a first-generation American who might not have had the opportunity to attend medical school in the 20th century, but by 2040, medical school had become significantly more affordable by shortening the time spent to 2.5 years and through funding from local counties and states to produce physicians who would serve their communities. Residency programs had also dramatically changed, transitioning from time-based to competency-based curricula, resulting in training lasting a variable number of years. Though the news Dr. Casillas delivers is heartbreaking, it is another example of the human connections made and compassionate care provided every day in emergency departments around the world.

In our imagined future, emergency departments have changed significantly since 2018. Technological advances like artificial intelligence (AI), remote patient monitoring, and telemedicine have increased access to care (particularly for underserved patients); allowed for earlier detection of life-threatening illnesses; and led to more precise triaging of patients before arriving at the emergency department. This has allowed emergency departments to anticipate and prepare for most patient arrivals and for board-certified emergency phy-

CONTINUED *on page 6*

2019 Course Topics

- Concussion - ED Essentials
- Importance of Coronary Risk Scores
- The ED's Role in Treating Opioid Addiction
- Important Pregnancy Factoids
- Learn to Love High Sensitivity Troponins
- Pediatric Fever - Part 1: Diagnostic Testing
- Pediatric Fever - Part 2: Taking It to the Bedside
- Stroke Guideline Controversies 2018 - Part 1
- Stroke Guideline Controversies 2018 - Part 2
- The Geriatric Emergency Department
- Serious Diseases, Outpatient Treatment - Part 1
- Serious Diseases, Outpatient Treatment - Part 2
- Cannabinoids in the ED
- Pediatric Thoracic Trauma
- 2019 Sepsis Update - Part 1
- 2019 Sepsis Update - Part 2
- The 2018 ATLS Guidelines: "What's New"?
- Trauma Care Controversies
- Pearls from *ED Leadership Monthly*
- Pearls from *Risk Management Monthly*
- Intravenous Fluid Controversies
- Pediatric Emergency Medicine Pearls - Part 1
- Pediatric Emergency Medicine Pearls - Part 2
- Telemedicine and the Emergency Physician
- Myths in Emergency Medicine
- The Consequences of Shift Work
- Visual Diagnosis Challenges - Part 1
- Visual Diagnosis Challenges - Part 2
- Important Recent EM Literature - Part 1*
- Important Recent EM Literature - Part 2*
- Optimizing ED Operations*
- Diagnostic and Therapeutic Controversies*

*Topics listed with an asterisk (*) are 90-minute faculty panel discussions; all other topics are 30 minutes.

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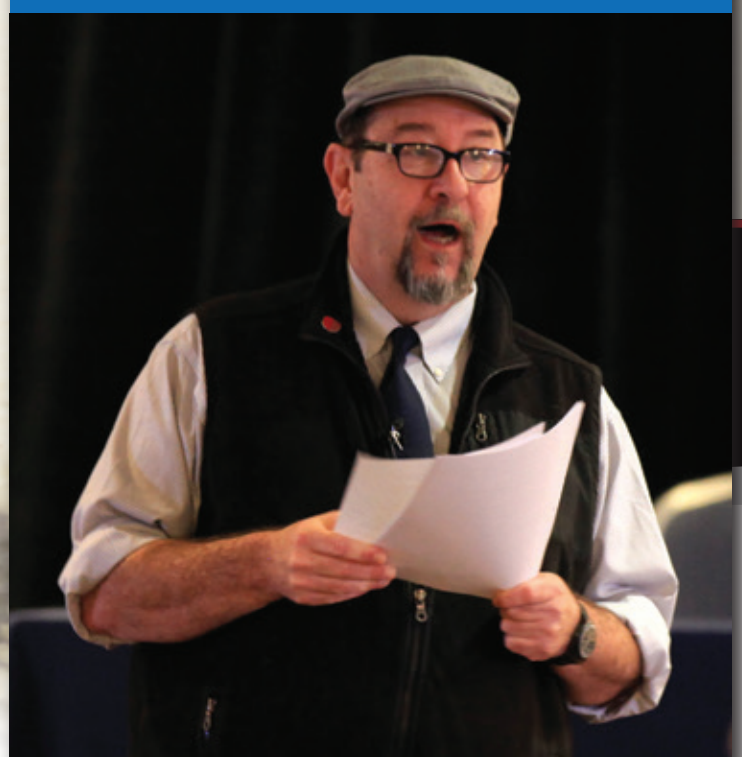

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sicians to perform medical screening exams remotely and schedule patients to see their primary care physician or a subspecialist if more suitable. The reimbursement landscape and the business model of emergency medicine have finally adapted to the world of value-based care, and emergency departments are actually being reimbursed for sending lower-acuity patients to primary care physicians and subspecialists.

Perhaps the biggest change has been the elimination of most inpatient general medicine beds in America. Based upon each patient's individual pharmacogenetic profile, robots start IVs, administer medications, and draw blood work at home, then drones transport these samples to labs for analysis. Due to physicians being able to remotely monitor patients' vital signs and clinical status, the need to admit patients has plummeted. This has resulted in the majority of America's acute care hospitals being closed. However, the need for emergency physicians has only grown, with micro-hospitals and freestanding emergency departments popping up from coast to coast, driven by the need for every community to have access to the acute care system as well as a desire to have a highly trained diagnostician physically evaluate patients in an increasingly digitized world.

A few hours later, Mr. Smith's clinical status starts to decline. He becomes more hypoxemic and tachypneic. The smart ultrasound wheels itself back to meet Mr. Smith in the resuscitation bay, and the AI software notices a dilated right ventricle with reduced tricuspid annular plane systolic excursion (TAPSE) consistent with a pulmonary embolism (PE). Dr. Casillas checks his advance directive through the national next-generation health information exchange prior to intubation and alerts his family members who had subscribed to his real-time care feed. The hype of medical informatics has been realized as patients' social, wearable, clinical, and genomic data are finally integrated into electronic medical records. A few minutes later he codes, and Dr. Casillas initiates extracorporeal membrane oxygenation (ECMO) and pushes tissue plasminogen activator nanobots, which have replaced the need for intravenous thrombolytics and catheter-directed thrombolysis. Initiating ECMO on a 72-year-old had become routine since the mid-2030s, when life expectancy surpassed 100. The AI resource allocation software then notices that, given his need for dedicated PE and ECMO teams, as well as local bed availability and risk-adjusted patient outcomes data, it would be best to transfer Mr. Smith to a hospital 90 miles away, bypassing three local centers. A minute later, he is loaded into an ICU drone equipped with tele-ICU capabilities and a midlevel critical care proceduralist, and he is whisked away. Because of the efficiencies of transferring patients to the nearest open bed available with appropriate resources rather than the closest hospital or the hospital that just so happened to be connected to the emergency department, the word "boarding" has been relegated to "back in my day" stories.

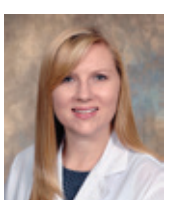
This futuristic thought experiment highlights two unique business models: micro-hospitals and hyper-acute specialty hospitals. In the emergency medicine of tomorrow, the latter, generally one every 100 miles, have been formed because in addition to the economies of scale within larger centers, a growing body of evidence had shown that high-volume centers, whether they be performing coronary artery bypass grafting or delivering ICU care, perform far better than lower-volume centers in terms of patient outcomes. A mix of large academic centers and corporations raced to consolidate the hospital market in the 2030s and created these 5,000-bed megaplexes of health care, just as Walmart and Amazon had done in the retail space during the early 2000s. Americans still needed access to acute care within a reasonable distance from their homes, and so the micro-hospital was born. Part freestanding emergency department with resuscitation bays and imaging in-house, part observation unit, and part heliport to efficiently ferry critical patients in specially made ICU drones to the specialty hyper-acute hospitals, these centers have proliferated, with emergency physicians at the helm.

While our specialty will evolve dramatically over the next 50 years, we believe the need for emergency physicians will only continue to grow. Tomorrow's emergency physicians will build upon the giants who founded emergency medicine by being diagnosticians who can make sense of all the noise generated from enhanced triaging and remote patient monitoring, availabalists who see patients 24-7-365, resuscitationists who bring people back from death's doorstep, and dispositionists who quarterback care in an increasingly hyper-specialized system. Most important, in an ever-virtualized world, they'll serve as the humanists who actually take a few minutes to sit down and talk to their patients, bringing an element of sanity to the chaos of 2068.

NOTE: The views represented in this futuristic thought experiment solely belong to the authors and do not represent those of EMRA.

DR. MANIYA is the President of EMRA and a resident at The Mount Sinai Hospital in New York.

DR. JAROU is the immediate Past President of EMRA and an administration fellow at the University of Chicago.



DR. HUGHES is the President-Elect of EMRA and a resident at the University of Cincinnati.

...Patient seems confused...soot around mouth...

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*Prior to administration of CYANOKIT, smoke inhalation victims should be assessed for exposure to fire or smoke in an enclosed area; presence of soot around the mouth, nose, or oropharynx; or altered mental status.[1]

IMPORTANT SAFETY INFORMATION

Cyanide poisoning may result from inhalation, ingestion, or dermal exposure. Prior to administration of CYANOKIT, smoke-inhalation victims should be assessed for: exposure to fire or smoke in an enclosed area; presence of soot around the mouth, nose, or oropharynx, and altered mental status. In addition to CYANOKIT, treatment of cyanide poisoning must include immediate attention to airway patency, adequacy of oxygenation and hydration, cardiovascular support, and management of any seizure activity.

Use caution in the management of patients with known anaphylactic reactions to hydroxocobalamin or cyanocobalamin. Consideration should be given to use of alternative therapies, if available. Allergic reactions may include: anaphylaxis, chest tightness, edema, urticaria, pruritus, dyspnea, and rash. Allergic reactions including angioneurotic edema have also been reported in postmarketing experience.

Acute renal failure with acute tubular necrosis, renal impairment and urine calcium oxalate crystals have been reported following CYANOKIT therapy. Monitor renal function for 7 days following CYANOKIT therapy.

Substantial increases in blood pressure may occur following CYANOKIT therapy. Elevations in blood pressure (≥180 mmHg systolic or ≥110 mmHg diastolic) were observed in approximately 18% of healthy subjects receiving hydroxocobalamin 5 g and 28% of subjects receiving 10 g.

Usage may interfere with some clinical laboratory evaluations. Also, because of its deep red color, hydroxocobalamin may cause hemodialysis machines to shut down due to an erroneous detection of a “blood leak.” This should be considered before hemodialysis is initiated in patients treated with hydroxocobalamin. Due to potential photosensitivity, patients should avoid direct sun until erythema resolves.

There are no adequate and well-controlled studies of CYANOKIT in pregnant women. CYANOKIT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Safety and effectiveness of CYANOKIT have not been established in pediatric patients.

The most common adverse reactions (>5%) included transient chromaturia, erythema, oxalate crystals in urine, rash (predominantly acneiform), increased blood pressure, nausea, headache, decreased lymphocyte percentage, and injection site reactions.

Please see Brief Summary of Prescribing Information on adjacent pages.

You are encouraged to report negative side effects of prescription drugs to the US Food and Drug Administration (FDA). Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Reference: 1. CYANOKIT (single 5-g vial) [package insert]. Columbia, MD: Meridian Medical Technologies, Inc.; 2017.

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CYANOKIT®
(hydroxocobalamin for injection)

BRIEF SUMMARY:

Consult full Prescribing Information for complete product information

Use with Other Cyanide Antidotes
Caution should be exercised when administering other cyanide antidotes simultaneously with Cyanokit, as the safety of co-administration has not been established. If a decision is made to administer another cyanide antidote with Cyanokit, these drugs should not be administered concurrently in the same intravenous line.

Incompatibility Information
Physical incompatibility (particle formation) and chemical incompatibility were observed with the mixture of hydroxocobalamin in solution with selected drugs that are frequently used in resuscitation efforts. Hydroxocobalamin is also chemically incompatible with sodium thiosulfate and sodium nitrite and has been reported to be incompatible with ascorbic acid. Therefore, these and other drugs should not be administered simultaneously through the same intravenous line as hydroxocobalamin.

Simultaneous administration of hydroxocobalamin and blood products (whole blood, packed red cells, platelet concentrate and/or fresh frozen plasma) through the same intravenous line is not recommended. However, blood products and hydroxocobalamin can be administered simultaneously using separate intravenous lines (preferably on contralateral extremities, if peripheral lines are being used).

WARNINGS AND PRECAUTIONS

Emergency Patient Management
In addition to Cyanokit, treatment of cyanide poisoning must include immediate attention to airway patency, adequacy of oxygenation and hydration, cardiovascular support, and management of any seizure activity. Consideration should be given to decontamination measures based on the route of exposure.

Allergic Reactions
Use caution in the management of patients with known anaphylactic reactions to hydroxocobalamin or cyanocobalamin. Consideration should be given to use of alternative therapies, if available.

Allergic reactions may include: anaphylaxis, chest tightness, edema, urticaria, pruritus, dyspnea, and rash.

Allergic reactions including angioneurotic edema have also been reported in postmarketing experience.

Renal Disorders
Cases of acute renal failure with acute tubular necrosis, renal impairment and urine calcium oxalate crystals have been reported. In some situations, hemodialysis was required to achieve recovery. Regular monitoring of renal function, including but not limited to blood urea nitrogen (BUN) and serum creatinine, should be performed for 7 days following Cyanokit therapy.

Blood Pressure Increase

Many patients with cyanide poisoning will be hypotensive; however, elevations in blood pressure have also been observed in known or suspected cyanide poisoning victims.

Elevations in blood pressure (180 mmHg or greater systolic or 110 mmHg or greater diastolic) were observed in approximately 18% of healthy subjects (not exposed to cyanide) receiving hydroxocobalamin 5 g and 28% of subjects receiving 10 g. Increases in blood pressure were noted shortly after the infusions were started; the maximal increase in blood pressure was observed toward the end of the infusion. These elevations were generally transient and returned to baseline levels within 4 hours of dosing.

Use of Blood Cyanide Assay
While determination of blood cyanide concentration is not required for management of cyanide poisoning and should not delay treatment with Cyanokit, collecting a pretreatment blood sample may be useful for documenting cyanide poisoning as sampling post-Cyanokit use may be inaccurate.

Interference with Clinical Laboratory Evaluations and Clinical Methods
Clinical Laboratory Evaluations
Because of its deep red color, hydroxocobalamin has been found to interfere with colorimetric determination of certain laboratory parameters (e.g., clinical chemistry, hematology, coagulation, and urine parameters). *In-vitro* tests indicated that the extent and duration of the interference are dependent on numerous factors such as the dose of hydroxocobalamin, analyte, methodology, analyzer, hydroxocobalamin concentration, and partially on the time between sampling and measurement.

Based on *in-vitro* studies and pharmacokinetic data obtained in healthy volunteers, the following table (Table 2) describes laboratory interference that may be observed following a 5 g dose of hydroxocobalamin. Interference following a 10 g dose can be expected to last up to an additional 24 hours. The extent and duration of interference in cyanide-poisoned patients may differ. Results may vary substantially from one analyzer to another; therefore, caution should be used when reporting and interpreting laboratory results.

Table 2: Laboratory Interference Observed with *In-Vitro* Samples of Hydroxocobalamin

LABORATORY PARAMETER			
Clinical Chemistry	**Hematology**	**Coagulation**	**Urinalysis**
No Interference Observed			
Calcium Sodium Potassium Chloride Urea GGT	Erythrocytes Hematocrit MCV Leukocytes Lymphocytes Monocytes Eosinophils Neutrophils Platelets		
Artificially Increased*			
Creatinine Bilirubin Triglycerides Cholesterol Total protein Glucose Albumin Alkaline phosphatase	Hemoglobin MCH MCHC Basophils		pH (with all doses) Glucose Protein Erythrocytes Leukocytes Ketones Bilirubin Urobilinogen Nitrite
Artificially Decreased*			
ALT Amylase			pH (with equivalent doses of <5 g)
Unpredictable			
Phosphate Uric Acid AST CK CKMB LDH		aPTT PT (Quick or INR)	
Duration of Interference			
24 hours with the exception of bilirubin (up to 4 days)	12-16 hours	24-48 hours	48 hours up to 8 days; color changes may persist up to 28 days

*10% or greater interference observed on at least 1 analyzer

Analyzers used: ACL Futura (Instrumentation Laboratory), AxSYM®/Architect™ (Abbott), BM Coasys110 (Boehringer Mannheim), CellDyn 3700® (Abbott), Clinitek® 500 (Bayer), Cobas Integra® 700, 400 (Roche), Gen-S Coultronics, Hitachi 917, STA® Compact, Vitros® 950 (Ortho Diagnostics)

Clinical Methods
Because of its deep red color, hydroxocobalamin may cause hemodialysis machines to shut down due to an erroneous detection of a “blood leak.” This should be considered before hemodialysis is initiated in patients treated with hydroxocobalamin.

Photosensitivity
Hydroxocobalamin absorbs visible light in the UV spectrum. It therefore has potential to cause photosensitivity. While it is not known if the skin redness predisposes to photosensitivity, patients should be advised to avoid direct sun while their skin remains discolored.

ADVERSE REACTIONS
Serious adverse reactions with hydroxocobalamin include allergic reactions, renal disorders and increases in blood pressure.

Clinical Studies Experience
Because clinical trials were conducted under widely varying conditions, adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice.

Experience in Healthy Subjects
A double-blind, randomized, placebo-controlled, single-ascending-dose (2.5, 5, 7.5, and 10 g) study was conducted to assess the safety, tolerability, and pharmacokinetics of hydroxocobalamin in 136 healthy adult subjects. Because of the dark red color of hydroxocobalamin, the two most frequently occurring adverse reactions were chromaturia (red-colored urine) which was reported in all subjects receiving a 5 g dose or greater; and erythema (skin redness), which occurred in most subjects receiving a 5 g dose or greater. Adverse reactions reported in at least 5% of the 5 g dose group and corresponding rates in the 10 g and placebo groups are shown in Table 3.

Table 3: Incidence of Adverse Reactions Occurring in >5% of Subjects in 5 g Dose Group and Corresponding Incidence in 10 g Dose Group and Placebo

	5 g Dose Group		**10 g Dose Group**	
ADR	**Hydroxocobalamin N=66 n (%)**	**Placebo N=22 n (%)**	**Hydroxocobalamin N=18 n (%)**	**Placebo N=6 n (%)**
Chromaturia (red colored urine)	66 (100)	0	18 (100)	0
Erythema	62 (94)	0	18 (100)	0
Oxalate crystals in urine	40 (61)	1 (4)	10 (56)	0
Rash*	13 (20)	0	8 (44)	0
Blood pressure increased	12 (18)	0	5 (28)	0
Nausea	4 (6)	1 (5)	2 (11)	0
Headache	4 (6)	1 (5)	6 (33)	0
Lymphocyte percent decreased	5 (8)	0	3 (17)	0
Infusion site reaction	4 (6)	0	7 (39)	0

*Rashes were predominantly acneiform

In this study, the following adverse reactions were reported to have occurred in a dose-dependent fashion and with greater frequency than observed in placebo-treated cohorts: increased blood pressure (particularly diastolic blood pressure), rash, nausea, headache and infusion site reactions. All were mild to moderate in severity and resolved spontaneously when the infusion was terminated or with standard supportive therapies.

Other adverse reactions reported in this study and considered clinically relevant were:

- *Eye disorders:* swelling, irritation, redness
- *Gastrointestinal disorders:* dysphagia, abdominal discomfort, vomiting, diarrhea, dyspepsia, hematochezia
- *General disorders and administration site conditions:* peripheral edema, chest discomfort
- *Immune system disorders:* allergic reaction
- *Nervous system disorders:* memory impairment, dizziness
- *Psychiatric disorders:* restlessness
- *Respiratory, thoracic and mediastinal disorders:* dyspnea, throat tightness, dry throat
- *Skin and subcutaneous tissue disorders:* urticaria, pruritus
- *Vascular disorders:* hot flush

Experience in Known or Suspected Cyanide Poisoning Victims

Four open-label, uncontrolled, clinical studies (one of which was prospective and three of which were retrospective) were conducted in known or suspected cyanide-poisoning victims. A total of 245 patients received hydroxocobalamin treatment in these studies. Systematic collection of adverse events was not done in all of these studies and interpretation of causality is limited due to the lack of a control group and due to circumstances of administration (e.g., use in fire victims). Adverse reactions reported in these studies listed by system organ class included:

- *Cardiac disorders:* ventricular extrasystoles
- *Investigations:* electrocardiogram repolarization abnormality, heart rate increased
- *Respiratory, thoracic, and mediastinal disorders:* pleural effusion

Adverse reactions common to both the studies in known or suspected cyanide poisoning victims and the study in healthy volunteers are listed in the healthy volunteer section only and are not duplicated in this list.

Postapproval Experience

The following adverse reactions have been identified during postapproval use of Cyanokit. Because adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency.

Cases of acute renal failure with acute tubular necrosis, renal impairment and urine calcium oxalate crystals have been reported in patients treated with Cyanokit.

DRUG INTERACTIONS

No formal drug interaction studies have been conducted with Cyanokit.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C. There are no adequate and well controlled studies of Cyanokit in pregnant women. In animal studies, hydroxocobalamin caused skeletal and visceral (soft tissue) abnormalities at exposures (based on AUC) similar to human exposures at the therapeutic dose. Cyanokit should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because cyanide readily crosses the placenta, maternal cyanide poisoning results in fetal cyanide poisoning. Timely treatment of the pregnant mother may be lifesaving for both mother and fetus.

In animal studies, pregnant rats and rabbits received Cyanokit (75, 150, or 300 mg/kg/d) during the period of organogenesis. Following intraperitoneal dosing in rats and intravenous dosing in rabbits, maternal exposures were equivalent to 0.5, 1, or 2 times the human exposure at the therapeutic dose (based on AUC). In the high dose groups for both species, maternal toxicity occurred, and there was a reduced number of live fetuses due to embryofetal resorptions. In addition, decreased live fetal weight occurred in high dose rats, but not in rabbits. Incomplete skeletal ossification occurred in both rats and rabbits. In rats, two fetuses of the high dose group and two fetuses of the mid dose group (each from a different litter) had short, rudimentary or small front or hind legs. Rabbit litters and fetuses exhibited a dose dependent increase in various gross soft tissue and skeletal anomalies. The main findings in rabbits were flexed, rigid flexor or medially rotated forelimbs or hindlimbs and domed heads at external examination; enlarged anterior or posterior fontanelles of the ventricles of the brain and flat, bowed or large ribs at skeletal examination; and dilated ventricles of the brain, and thick wall of the stomach at visceral examination.

Labor and Delivery

The effect of Cyanokit on labor and delivery is unknown.

Nursing Mothers

It is not known whether hydroxocobalamin is excreted in human milk. Cyanokit may be administered in life-threatening situations, and therefore, breast-feeding is not a contraindication to its use. Because of the unknown potential for adverse reactions in nursing infants, the patient should discontinue nursing after receiving Cyanokit.

Pediatric Use

Safety and effectiveness of Cyanokit have not been established in this population. In non-US marketing experience, a dose of 70 mg/kg has been used to treat pediatric patients.

Geriatric Use

Approximately 50 known or suspected cyanide poisoning victims aged 65 or older received hydroxocobalamin in clinical studies. In general, the safety and effectiveness of hydroxocobalamin in these patients was similar to that of younger patients. No adjustment of dose is required in elderly patients.

Renal Impairment

The safety and effectiveness of Cyanokit have not been studied in patients with renal impairment. Hydroxocobalamin and cyanocobalamin are eliminated unchanged by the kidneys.

Hepatic Impairment

The safety and effectiveness of Cyanokit have not been studied in patients with hepatic impairment.

OVERDOSAGE

No data are available about overdose with Cyanokit in adults. Should overdose occur, treatment should be directed to the management of symptoms. Hemodialysis may be effective in such a circumstance, but is only indicated in the event of significant hydroxocobalamin-related toxicity. Because of its deep red color, hydroxocobalamin may interfere with the performance of hemodialysis machines.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of hydroxocobalamin. Hydroxocobalamin was negative in the following mutagenicity assays: *in-vitro* bacterial reverse mutation assay using *Salmonella typhimurium* and *Escherichia coli* strains, an *in-vitro* assay of the tk locus in mouse lymphoma cells, and an *in-vivo* rat micronucleus assay.

The effect of hydroxocobalamin on fertility has not been evaluated.

PATIENT COUNSELING INFORMATION

Cyanokit is indicated for cyanide poisoning and in this setting, patients will likely be unresponsive or may have difficulty in comprehending counseling information.

Erythema and Chromaturia

Patients should be advised that skin redness may last up to 2 weeks and urine coloration may last for up to 5 weeks after administration of Cyanokit. While it is not known if the skin redness predisposes to photosensitivity, patients should be advised to avoid direct sun while their skin remains discolored.

Rash

In some patients, an acneiform rash may appear anywhere from 7 to 28 days following hydroxocobalamin treatment. This rash will usually resolve without treatment within a few weeks.

Renal Disorders

Patients should be advised that renal function will be monitored for 7 days following treatment with Cyanokit or, in the event of renal impairment, until renal function returns to normal.

Pregnancy and Breast-feeding

Patients should be advised that maternal cyanide poisoning results in fetal cyanide poisoning. Treatment for cyanide poisoning may be lifesaving for both mother and fetus. Patients should notify their physician if they were pregnant during therapy with Cyanokit. It is not known whether hydroxocobalamin is excreted in human milk.

This brief summary is based on CYANOKIT® (hydroxocobalamin for injection) Prescribing Information Version 180_US_20171_NO, Issued: June 2017. For current package insert and further product information, please visit www.cyanokit.com or call Pfizer Medical Information toll-free at 1-800-438-1985.

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Medication-Assisted Therapy

It's more than just buprenorphine

by EVAN SCHWARZ, MD, FACEP, FACMT; AND R. COREY WALLER, MD, MS, FACEP, DFASAM

Editor's Note: This is the sixth part of an ongoing series on what emergency physicians can do to combat the opioid epidemic.

Plenty has been written and said about buprenorphine recently, and that's not a bad thing.[1–3] It's a medication that can be started from the emergency department under the correct circumstances. It's also a medication that a lot of us probably weren't very familiar with, so many likely benefited from a crash course on bup. Of course, it is important to remember that medication-assisted therapy (MAT) involves more than just buprenorphine. In fact, there are two other medications patients can choose: methadone and naltrexone. Are emergency physicians likely to start patients on either of these medications from the emergency department? Absolutely not, although from what I'm told, some emergency departments have been using intramuscular methadone for opioid withdrawal for quite some time. Either way, given the emphasis on treatment of opioid use disorder (OUD) with medications, there is a fair chance we'll start seeing more patients on these agents. As such, it is important that we have a basic understanding of them and how they could affect emergency physicians' practice.

Also, it is worth noting that while we'll continue to use the term MAT because most of us are familiar with it, the term is falling out of favor because some feel it inappropriately deemphasizes the role that medication plays in recovery for this population.

Methadone

Methadone has been the mainstay in the treatment of OUD long before buprenorphine became the cool kid on the block. While there is a ton of stigma associated with it and the word swirls with all sorts of negative connotations, methadone has been very successful in treating patients with OUD.[4] It is a full agonist without a ceiling effect like buprenorphine, which means that it can be particularly dangerous. This is one reason it is so tightly regulated, at least for addiction. While it can be prescribed for pain, it cannot be prescribed for addiction. Patients must go to a properly licensed treatment center (e.g., a methadone clinic) where it can be dispensed under a physician's supervision.

At the clinic, methadone is generally dispensed once a day, although toward the end of pregnancy, patients may receive twice-per-day dosing. If you're boarding a patient with an OUD, don't be fooled if they tell you that they get the medication three times per day, which a few of my floor patients have tried in the past. If the center is open or has an on-call number, you can verify the dose and frequency.

What about just doing a quick search of the prescription drug monitoring program (PDMP)? This seems easier than trying to hunt down the methadone clinic and awaiting a return call. Unfortunately, this won't work. Since methadone is dispensed by these facilities, no prescription is ever written. While this may seem like semantics, it means this information is never loaded into the PDMP, so it won't be there when you search. Sensing this was a problem, the ACEP Council passed a resolution in 2018 to have methadone included in the PDMP.[5]

As mentioned previously, methadone must be respected. It is potent, with a very long half-life, which means it can easily cause respiratory depression. Commonly, this occurs on days two through four if the medication is titrated too quickly. Fortunately, it doesn't necessarily require large doses of naloxone to reverse it. In fact, 0.04 mg of naloxone may be enough.[6] Patients can recrudesce, and this does not always happen quickly. I've had a quite a few who went down even four hours after their first dose of naloxone. These patients will require prolonged observation and possibly a naloxone infusion.

Keep in mind that the standard urine drug screen does not pick up methadone and can't be relied on to rule out a methadone overdose. It won't pick up buprenorphine or fentanyl either, making this test even more useless.

Methadone also causes a prolonged QTc. Does this mean everyone on methadone needs an ECG? No, it does not, and at low doses, such as 20–40 mg/day, methadone probably does not have a significant effect.[7] However, some patients are on doses of more than 100 mg/day. In this case, you may want to consider an alternative to medications in the emergency department that cause QTc prolongation or at least obtain an ECG prior to ordering these medications.

What about your patient on methadone that is NPO? I'd recommend cutting the oral dose by at least half.[8,9] For patients on methadone with acute pain, the dose should not be increased in the emergency department. In future columns, we'll tackle acute pain control in patients on MAT.

Naltrexone

Naltrexone is completely different than methadone or buprenorphine; it is a complete antagonist at the mu receptor. Think of it as extended-release naloxone. While there is an oral form, almost all patients will be on the injectable form, which is meant to last a month to help with compliance. With its high binding affinity to the mu receptor, it works by preventing patients from getting high if they try to use while on the medication. There is no euphoria associated with it, and at least initially, it won't help with cravings.

Patients must abstain from all opioids for at least seven to 10 days prior to receiving naltrexone. If they do not, the drug can precipitate severe opioid withdrawal. Unlike naloxone, which should improve after 40 to 60 minutes, or buprenorphine, which can be overcome by giving more buprenorphine, this effect of naltrexone can last a long time. Remember the injectable form can last 30 days, but the withdrawal should not last nearly this long.

While precipitated withdrawal is the main complication we worry about with naltrexone, there are also reports of agitated delirium following the administration of it in patients who recently used an opioid.[10,11] Otherwise, it is very safe unless patients try to overcome the blockade with either very large doses or very potent opioids, or they relapse but now have very little tolerance.

It's important to mention that there are other indications for naltrexone. It is used in patients with alcohol use disorder due to the effects of mu receptors on our reward system. There is also a weight-loss pill that is a combination of bupropion and naltrexone. This isn't a huge problem, unless someone doesn't obtain a complete history and prescribes it to an opioid-dependent patient. We've had at least one patient to whom this happened, and it took large amounts of fentanyl and multiple antiemetics to improve her symptoms. We've also recently noticed a few physicians using low-dose naltrexone for chronic pain.[12,13]

What About Lofexidine?

You may have also heard of a new, recently approved drug indicated for opioid withdrawal, lofexidine. It's actually been used in Europe for years. Alas, it is just an α-2 agonist, very similar to (and much more expensive than) clonidine. It is not used for MAT.

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SEND US YOUR QUESTIONS!

If you have questions or ideas, feel free to send them our way at schwarze@wustl.edu. Until then, let data, science, and math rule the day!

A Pioneer of EM

Dr. John Lumpkin has dedicated his career to serving our patients in the hospital, halls of government, and community

Although John R. Lumpkin, MD, MPH, FACEP, FACME, FAAN, was initially drawn to a career in biophysics, his desire to combine a love of science with a need to help people caused him to shift his focus to medicine. An evening working with a family friend in the emergency department at Oak Park Hospital in Oak Park, Illinois, cemented his interest in emergency medicine. A few years later, in 1976, he became the first African American emergency medicine resident, training at the University of Chicago under Peter Rosen, MD. After finishing residency, he joined the emergency medicine faculty at the University of Chicago.

Early in his career, he recognized the importance of government and politics in serving the needs of emergency physicians and their patients. He worked on key emergency medical services legislation in Illinois and went on to serve as director of the state's Department of Public Health under three different governors.

Andrea Green, MD, FACEP

He has also been an active member of the Illinois College of Emergency Physicians and ACEP for most of his career, serving in many leadership positions in both organizations. He served as Speaker of the ACEP Council from 1985 to 1987 and on the ACEP Board of Directors from 1987 to 1993, and he was the first African American to hold either position.

Dr. Lumpkin recently sat down with Andrea Green, MD, FACEP, an emergency physician and Chair of ACEP's Diversity, Inclusion, and Health Equity Section, to discuss his career, his accomplishments, and his vision for the future of emergency medicine leadership. Here are some highlights from that discussion.

JOHN LUMPKIN

John R. Lumpkin, MD, MPH, FACEP, FACME, FAAN

AG: John, your background and career have been impressive. What have been some of your guiding principles?

JL: I guess the best way to describe me is that I'm a believer in the ultimate goodness of my fellow man. I believe that I am a person who's dedicated to service of my fellow man. That has been something that has guided me throughout my entire life, from my days in high school through my current career.

AG: Could you describe for us the career journey that you chose based on the way that you wanted to live your life and help other people?

JL: As I was growing up, I was always very interested in math and science. As I was going through high school, I said, "Well, I think I want to be a scientist. I'd like to be a biophysicist," because I liked biology, physics, and chemistry. When I went off to school, my first year at MIT, I began to realize that so much was going on in the world with the war in Vietnam and the civil rights movement, and if I actually became a biophysicist, I would spend all my life in the laboratory. I wanted to have an impact upon people and their lives. At that point, I knew I wanted to go to medical school and was fortunate to get into Northwestern.

My freshman year of medical school, I spent Christmas Eve working with Vera Markovin, MD, who was one of the early founders of the Illinois College of Emergency Physicians. She was a family friend, and it was that evening in 1971 that really got me interested in emergency medicine.

As I went through medical school, I really designed my career to do two things: one, to begin to take courses that would better prepare me to go into emergency medicine and, two, maintain my contacts. I was working with the Medical Committee for Human Rights and other organizations. I was fortunate to be able to join the emergency medicine residency at the University of Chicago and to train under Peter Rosen, MD.

While I was training as a resident, I worked with Harold Washington's campaign; he was running for mayor in Chicago.

The Illinois Emergency Medical Services Systems Act was up for approval, and I assisted the chapter with it. Because of my activities on that, I was appointed chair of the EMS council by Illinois Gov. James R. Thompson, and I began to have more and more experience with government and governmental bodies.

It was at that point in my career that I felt I needed to have more training because, as every emergency physician knows, the things that bring people into the emergency department often aren't their clinical problems.

I went on to get a master's degree in public health. One of the people I had worked with, who subsequently became the director of the Department of Public Health in Illinois, invited me to come in as a deputy director. When

CONTINUED *on page 12*

> I think it's really critical for emergency physicians to avoid seeing themselves as someone just showing up for a shift, but to recognize they're part of a broader system.
>
> *–John R. Lumpkin, MD, MPH, FACEP, FACME, FAAN*

he left, I was appointed director, first under Gov. Thompson, then Gov. Jim Edgar, and then finally, Gov. George Ryan. I served in that position for 12 years. Throughout that time, my own personal identity was that I was an emergency physician first, and that always influenced me as I thought about my career.

AG: Tell us a little bit about how you decided to pursue positions of leadership within ACEP.

JL: I started my career in ACEP with the Illinois College of Emergency Physicians. I joined the board of directors of the Illinois College, and I became the President-Elect and then the President of the Illinois College. I was very active in academic emergency medicine. I served as Chair of the Society of Teachers of Emergency Medicine while I was at the University of Chicago. That organization was one of the precursors for the Society for Academic Emergency Medicine. They merged with the University Association for Emergency Medicine to form the Society for Academic Emergency Medicine. I was active in a number of committees of the College. I chaired a committee that was established to determine the length and content for residencies in emergency medicine. In 1983, I was elected as Vice Speaker of the ACEP Council, and then, two years later, I was elected Speaker of the Council. I went on to the Board of Directors, where I served for two terms.

AG: Is there anything that you would tell someone who is preparing themselves for becoming a leader?

JL: The first thing I would say, and I believe this is a quote from Woody Allen, is "80 percent of success in life is showing up." The role of ACEP is to do two things: protect the best interest of the patients that we serve and protect the specialty. There's a third: to be concerned about those who commit themselves to providing emergency services as emergency physicians. Not only is it showing up, but I think my success has been related to benefiting from my commitment and service to the Colleges of Emergency Physicians.

AG: What role do you see for emergency medicine or emergency physicians in helping to address health disparities in our day-to-day encounters with patients and our operations?

JL: I think it's really critical for emergency physicians to avoid seeing themselves as someone just showing up for a shift but to recognize they're part of a broader system.

The emergency department and emergency physicians are in an ideal position to go beyond their shifts and be engaged with hospital administration, and also with the community, to think about that visit and that person in the emergency department as someone who is disconnected, and understanding that the emergency department can play a critical role in connecting them. The emergency physician becomes the connector, the pivot point, that can make the difference between someone chronically using the emergency department day after day and someone who actually is living a better life. I think our responsibility as emergency physicians is to think about the whole patient.

AG: What do you see as factors that could help move the needle successfully in solving some of the issues that we face?

JL: I think the factors that need to be addressed are both internal and external to the emergency department. First, there's clear evidence that physicians and everyone in our society have biases and stereotypes. There's clear evidence that the longer you work on a shift, the more likely you are to use those biases in decision making. I think it's important for emergency physicians to understand how this occurs and to develop systems, including the use of electronic health records, to improve medical decision making.

The second is recognizing the issues that impact patients' lives. For us in emergency medicine, we need to recognize that we can have an impact on those issues by being an advocate for those patients, and being an advocate not just to make sure that they get the best care but being advocates for the goal to create the environment where everyone has a fair and just opportunity to be as healthy as possible.

AG: Tell me a little bit about your role in the Robert Wood Johnson Foundation.

JL: I'm one of two program senior vice presidents. We're responsible for the various programs that are supported and funded by the Robert Wood Johnson Foundation. My specific role is to oversee our work related to developing leadership, engaging business, and transforming health and health care systems.

We are seeking to change the environment but also to have health care coordinate with public health and social services so that the needs—not only in the clinical setting but where people live, learn, work, and play—are addressed.

AG: Can you highlight some of your accomplishments?

JL: When I look back on my career, I hope I've contributed to the specialty through leadership, and one of my high points was being both Speaker and on the Board of Directors of the College and being the first African American to do that.

AG: I thank you so much for not only taking the time today but also for the inspiration that you've been and the example you've set for so many, particularly minorities in the field of emergency medicine.

ILLUSTRATION: CHRIS WHISSEN & SHUTTERSTOCK.COM

BEDSIDE EDUCATION

Atrial Fibrillation at Club Ventricle

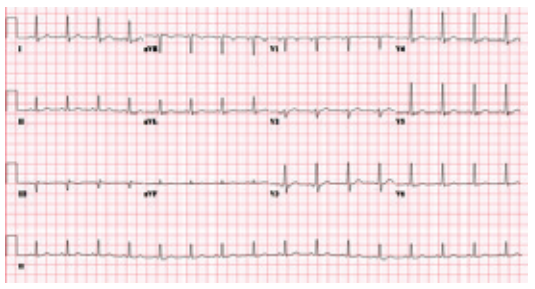
A dance club analogy—can you feel the beat?

by TRENT STEPHENSON, DO, FACEP

Have you ever thought of the cardiac conduction system as a night club—Club Ventricle? Who knows, you might have to stop yourself from busting a move the next time you're assessing atrial fibrillation in your emergency department!

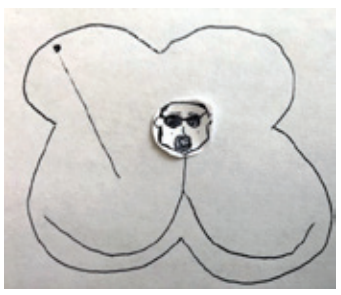
Atrial Fibrillation

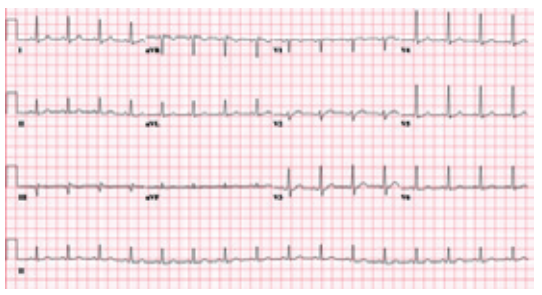
Atrial fibrillation has an atrial rate of 300–600 bpm. Picture it as 300–600 people trying to get into a club (ventricle). The atrioventricular (AV) node (bouncer) is only able to let 140–160 bpm (people) into the club at a time, and the rate is irregular. All beats (people) are going through the same point of entry, so all beats are the same width.



Wolff-Parkinson-White Syndrome (WPW)

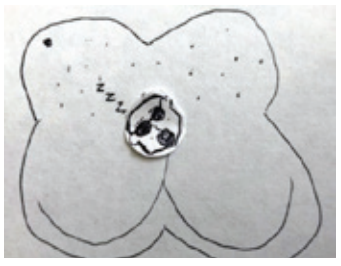
In WPW, beats are being conducted by an accessory pathway (the side door of the club) and not going through the AV node (bouncer). The side door of Kent is farther from the dance floor, so the QRS complex is wider as the people travel farther and do a dance move called the Delta Wave. Travel distance and dance moves take time.

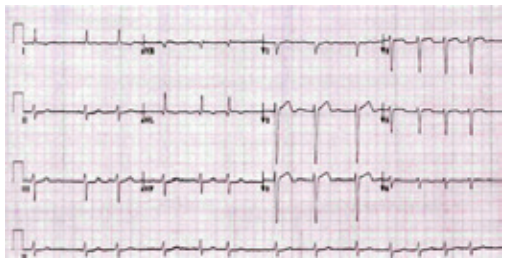




Atrial Fibrillation with Rapid Ventricular Response (RVR) After AV Nodal Blocking Agent

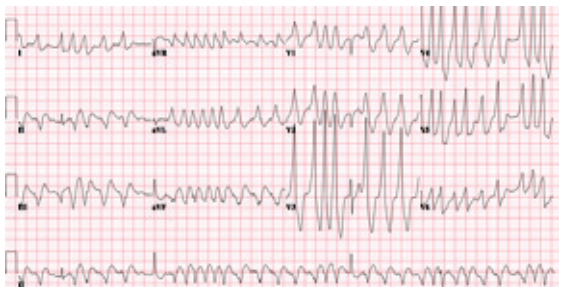
The AV node (bouncer) is inhibited. Now, fewer beats (people) will get into Club Ventricle because the bouncer is slower checking IDs and collecting a cover charges and cannot clear people as fast.





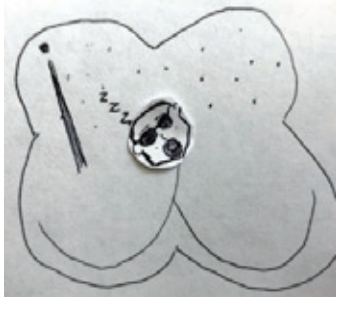
Atrial Fibrillation with RVR in a Patient with WPW

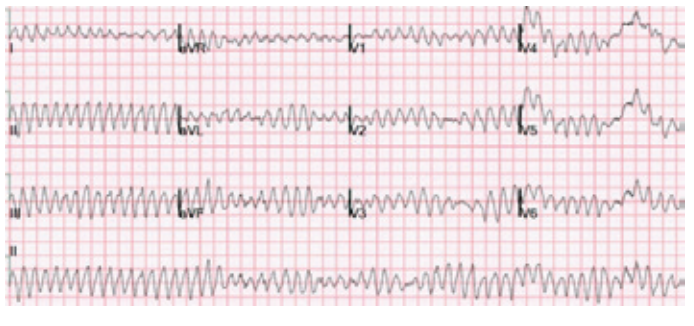
Some beats (people) are going through the main door with the AV node (bouncer). Those are the "straight and narrow" people, so the QRS complex will be narrower. Some beats (people) are going through the side door of Kent, and their path/QRS interval is wider. This sparks a dance competition in Club Ventricle with different QRS intervals (dance moves).



Atrial Fibrillation with RVR and WPW After an AV Nodal Blocking Agent Has Been Given

The AV node (bouncer) is inhibited by AV nodal blocking agents, so the beats (people) become impatient. Instead of waiting in line to go through the main door, they rush for the side door, which is now a faster point of entry. The club gets "turnt up" for a while but then gets shut down (ventricular fibrillation arrest).





Treatment Options for Atrial Fibrillation with RVR and WPW

- **Procainamide** acts like club security, running to the side door to slow down patrons from sneaking in. It prolongs the refractory period of the accessory pathway.
- **Cardioversion** acts as a strobe light that lowers the seizure threshold of the partygoers and resets them after a short post-ictal period, bringing order to the club.

TAKE-HOME POINTS

- When dealing with atrial fibrillation, look closely at the widths of the QRS complexes. If they are different widths, then consider that an accessory pathway is being used in addition to the beats being transmitted through the AV node.
- Look at the rate of atrial fibrillation. If the rate is 200–300 bpm at times, then also consider an accessory pathway.
- Do not use AV nodal blocking agents in atrial fibrillation with RVR in the presence of WPW, as it allows the accessory pathway to take over.
- Use procainamide or consider cardioversion in patients with atrial fibrillation with RVR and WPW.
- The Delta Wave is an amazing dance move and can be used at most social events. Be cautious—you may get cardioverted!

DR. STEPHENSON is an emergency physician with Integrative Emergency Services in Dallas.

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DR. DARK is assistant professor of emergency medicine at Baylor College of Medicine in Houston and executive editor of PolicyRx.org.

Health IT—Good or Bad?

Either way, IT has permanently changed the health care landscape

by CEDRIC DARK, MD, MPH

Even with the significant investments made by the federal government, hospitals, and physicians over the past 10 years, it is critical to remember that health information exchange is an evolution, not a revolution.[1] The migration from paper to electronic records has been fraught with difficulty, resulting in decreased productivity among physicians during implementation and clunky user interfaces and possibly contributing to burnout—but it has changed the practice of medicine for good. Instead of making clinical care easier, physicians now only spend 49 percent of their time with patients. The majority of their time is spent striking the keys behind the computer.[2]

Physicians truly display a love-hate relationship with health information technology in the clinical setting. On one hand, charts are legible, it is easy to look up old visits, and macros make documentation easier. On the other, there is an inordinate amount of useless text in the notes; the system is built for billing, not medical care; and it is nearly impossible to figure out how to order an insulin drip these days.

Yet the electronic takeover of health care does come with some tangible benefits to patients and to the overall health care system. Two recently reviewed studies, applicable to health information exchange in the emergency department setting, demonstrate shorter emergency department visits and decreased utilization of CT scans, MRIs, radiographs, and hospital admission.[3,4]

According to the ACEP revised policy, "Health Information Technology Standards," emergency physicians demand "seamless integration of data" and request that patient information is available in a "timely, usable, and secure manner."[5] As these data demonstrate, when these goals are achieved by an electronic health record, patient visits are more efficient and less costly. Patients faced charges that were nearly $1,200 lower when clinicians used the electronic medical record (EMR) than with paper records.

ACEP additionally recommends that its members become proponents of interoperable systems prior to institutions implementing expensive platforms that do not suit the needs of emergency physicians. If there is a system you think is especially useful, let your C-suite know about it before it invests in a product that will relegate you to being a disgruntled data-entry monkey.

Policymakers, hospital executives, and EMR entrepreneurs should all heed the words of Louis Yu, MD, MA, from our EMRA+PolicyRx Health Policy Journal Club: "Better, faster, and more interconnected systems for information exchange have the potential to make a difference in patient care and in the cost of care provided."[6] Another EMRA+PolicyRx Health Policy Journal Club article, reprinted here, examines the effect of health information exchanges on several patient-oriented outcomes.

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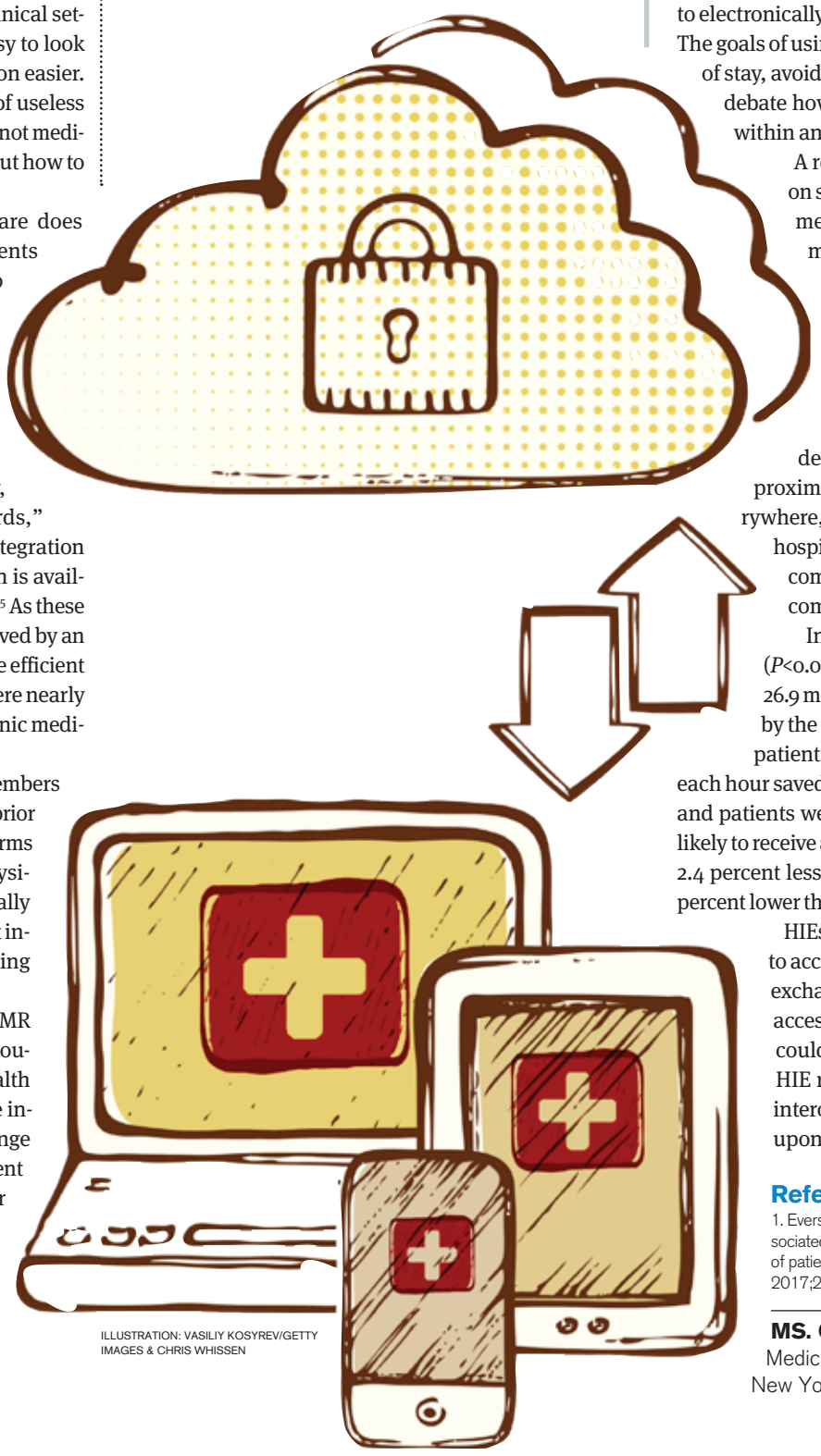

ILLUSTRATION: VASILIY KOSYREV/GETTY IMAGES & CHRIS WHISSEN

EMRA+POLICYRx HEALTH POLICY JOURNAL CLUB

Health Information Exchanges Have the Potential to Save Utilization and Cut Costs

by ERICA GOLDSTEIN

Since the passage of the Affordable Care Act (ACA), there have been substantial investments in developing health information exchanges (HIEs) to electronically transfer medical records between health care providers. The goals of using exchanges are to minimize service duplication, length of stay, avoidable admissions, and associated costs. However, studies debate how effective HIEs have been on reaching these goals both within and outside of the emergency department.

A recent study was designed to determine the effect of HIEs on six outcomes: length of stay in the emergency department, medical charges, hospitalization rates, and use of three modes of imaging (CTs, MRIs, and X-rays).[1] A unit clerk would fill orders for medical records by either requesting records electronically from hospitals with compatible HIEs or calling to request medical records be faxed, which were then scanned and uploaded.

The study analyzed the use of an HIE within the University of Michigan Health System (UMHS) emergency departments. The UMHS emergency departments have approximately 100,000 visits annually and have Epic's Care Everywhere, the HIE system used by approximately 20 percent of US hospitals. Of the requests made by HIE, 72 percent (n=566) were completed. Eighty-four percent of fax requests (n=3,082) were completed.

Information from HIEs was returned 51.0 minutes faster (P<0.001), translating to an emergency department visit that was 26.9 minutes shorter (P=0.099). No other outcomes were affected by the use of Care Everywhere. However, the time it took retrieve patient information, regardless of method, was significant. For each hour saved, emergency department visits were 52.9 minutes shorter and patients were 2.5 percent less likely to receive a CT, 1.6 percent less likely to receive an MRI, 2.4 percent less likely to receive a radiograph, and 2.4 percent less likely to be admitted (P<0.001 for all). Charges were 6.3 percent lower than average, resulting in savings of $1,187 per visit ($P$<.001).

HIEs provide benefit only to the extent that they decrease time to access medical records. Thus, efforts to improve information exchange should focus on improving the speed of health record access. It should also be noted that only 18 percent of requests could be made using Care Everywhere and only 72 percent of HIE requests made were completed. Therefore, universality, interoperability, and completion of requests are other factors upon which vendors should improve.

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MS. GOLDSTEIN is a dual-degree student at NYU School of Medicine and the Wagner Graduate School of Public Service in New York City.

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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).

DOACs for Cancer-Associated VTE

Are they better than LMWH?

by KEN MILNE, MD, MSC, CCFP-EM, FCFP, FRRMS

The Case

A 73-year-old man currently undergoing chemotherapy for colon cancer presents to the emergency department with a swollen right leg. His vital signs are all stable, and his leg does not look like it has cellulitis. The ultrasound confirms your suspicion of a deep-vein thrombosis (DVT). The patient is being prepared for outpatient management, but does not want to be on injections for the next six to 12 months. He asks if there are any other treatments besides low-molecular-weight heparin (LMWH).

Background

Cancer increases the risk of venous thromboembolism (VTE). Patients with cancer can be difficult to manage due to the higher risk of bleeding and the higher rate of thrombosis recurrence. The CLOT trial established LMWH as the standard therapy for symptomatic and asymptomatic VTE.[1]

Direct oral anticoagulants (DOACs) like rivaroxaban have been shown to be effective treatments for VTE without causing increased bleeding complication rates in non-cancer patients. A trial by Bean et al suggested it was safe and effective to dry start DOACs (no LMWH needed) in certain patients with VTE.[2]

Although DOACs are frequently used in the treatment of cancer-associated VTE, there is little evidence to support this practice. The SELECT-D trial was a small open-label pilot trial looking at the use of rivaroxaban. It showed a lower hazard ratio (HR) for VTE with wide confidence intervals and a higher clinically relevant non-major bleeding rate.[3]

Clinical Question

In cancer-associated VTE, is edoxaban noninferior to LMWH?

Reference

Raskob GE, van Es N, Verhamme P, et al. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med*. 2018;378(7):615-624.

- **Population:** Adult patients with active cancer or cancer diagnosed within the previous two years with acute symptomatic or asymptomatic VTE.
  - » **Exclusions:** See the article's supplementary appendix at https://www.nejm.org/doi/suppl/10.1056/NEJMoa1711948/suppl_file/nejmoa1711948_appendix.pdf.
  - » **Intervention:** LMWH for five days followed by oral edoxaban 60 mg daily for at least six months.
- **Comparison:** Subcutaneous (SQ) dalteparin 200 IU/kg daily (maximum 18,000 IU) for one month followed by 150 IU/kg daily for at least five months.
- **Outcome:**
  - » **Primary:** Composite of recurrent VTE or major bleeding during 12-month follow-up.
  - » **Secondary:** Clinically relevant nonmajor bleeding (CRNB), event-free survival, VTE-related death, all-cause mortality, recurrent DVT, recurrent pulmonary embolism. (The complete list is in the article's supplementary appendix.)

TABLE 1: SECONDARY OUTCOMES

	EDOXABAN	DALTEPARIN	HAZARD RATIO (95% CI)
Recurrent Venous Thromboembolism	41 (7.9%)	59 (11.3%)	0.71 (0.48–1.06); *P*=0.09
Recurrent Deep Vein Thrombosis	19 (3.6%)	35 (6.7%)	0.56 (0.32–0.97)
Recurrent Pulmonary Embolism	27 (5.2%)	28 (5.3%)	1.00 (0.59–1.69)
Major Bleeding	36 (6.9%)	21 (4.0%)	1.77 (1.03–3.04); *P*=0.04
Clinically Relevant Non-Major Bleeding	76 (14.6%)	58 (11.1%)	1.38 (0.98–1.94)
All-Cause Mortality	206 (39.5%)	192 (36.6%)	1.12 (0.92–1.37)
Event-Free Survival	287 (55%)	296 (56.5%)	0.93 (0.77–1.11)

Authors' Conclusions

"Oral edoxaban was noninferior to subcutaneous dalteparin with respect to the composite outcome of recurrent venous thromboembolism or major bleeding. The rate of recurrent venous thromboembolism was lower but the rate of major bleeding was higher with edoxaban than with dalteparin."

Key Results

The trial enrolled 1,046 patients and used a modified intention-to-treat analysis. The average patient age was the early 60s and more than 50 percent had metastatic disease, with 30 percent having recurrent cancer. Edoxaban was found to be noninferior to LMWH for the primary outcome of recurrent VTE or major bleeding.

- **Primary Outcome:** Recurrent VTE or major bleeding.
  - » 12.8 percent versus 13.5 percent; HR, 0.97 (95% CI, 0.70 to 1.36; *P*=0.006 for non-inferiority)
- **Secondary Outcomes:** See Table 1.

Evidence-Based Medicine Commentary

1. **Lack of Blinding:** Patients were aware of group allocation, while the outcome assessors for major bleeding were blinded. It is unclear whether the lack of patient blinding would have affected the results. The researchers could have minimized this bias by having placebo pills and SQ injections as controls.
2. **Primary Outcome:** The researchers created a composite outcome of efficacy (VTE recurrence) and safety (major bleed). Why not just have one primary outcome? Would the patients value the lower VTE rate with edoxaban (7.9 percent versus 11.3 percent) more or the lower major bleed rate (6.9 percent versus 4.0 percent) with LMWH? There was no statistical difference in all-cause mortality or event-free survival. They could have asked the patients a priori what they felt the most important outcome was, powered the study for this outcome, and considered all the rest as secondary outcomes.
3. **Changes to Endpoint and Time Frame:** The original trial design had co-primary outcomes for VTE recurrence and clinically relevant bleeding. This was changed to a composite outcome of VTE recurrence and major bleeding event.

   The researchers also extended the time frame from six to 12 months. The original primary outcomes at six months are not listed in the publication and can only be found in the supplementary appendix.

   These results showed noninferiority of edoxaban compared to LMWH for recurrent VTE (6.5 percent versus 8.8 percent; HR 0.75 [95% CI, 0.48–1.17]), but an increase in clinically relevant bleeds (15.9 percent versus 10.7 percent; HR 1.54 [95% CI, 1.10–2.16]). There was no difference in all-cause mortality or event-free survival.
4. **Noninferiority:** This trial was designed to see if oral edoxaban was not worse (noninferior) than LMWH. What about patient satisfaction of an oral medication compared to a daily injection? There was also no mention of cost, which may play a role in determining noninferiority.
5. **Conflicts of Interest:** The authors reported multiple conflicts of interest, and the trial was sponsored by the maker of edoxaban. The pharmaceutical company, in collaboration with the coordinating committee, was responsible for the trial design, protocol, and oversight, as well as collection and maintenance of the data. It also performed all the statistical analysis in collaboration with the writing committee. This does not make the data wrong but should make us more skeptical.

Bottom Line

It may be reasonable to discuss oral edoxaban with patients as a potential treatment for cancer-associated VTE. However, the decision should probably be left up to the patient and their oncologist.

Case Resolution

The patient is given LMWH and has outpatient injections arranged. He is referred back to his oncologist to further discuss the issue of using a DOAC to manage his cancer-associated DVT.

Thank you to Dr. Anand Swaminathan, assistant professor of emergency medicine at the St. Joseph's Regional Medical Center in Paterson, New Jersey.

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

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Q&A ABOUT OUR LITTLEST PATIENTS

KIDS KORNER

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DR. CANTOR is professor of emergency medicine and pediatrics, director of the pediatric emergency department, and medical director of the Central New York Regional Poison Control Center at Upstate Medical University in Syracuse, New York.

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.

IV Fluids for Lumbar Puncture Success

Question 1: In neonates and infants, does an IV fluid bolus prior to lumbar puncture (LP) improve success rate?

Admit it—unsuccessful LPs in neonates and infants are really frustrating. While a number of factors play a role in the likelihood of a successful LP, does an IV fluid bolus actually increase the size of the subarachnoid space and possibly improve LP success rate?

Interestingly, we were only able to find a single study addressing this question. It was a prospective, observational study by Rankin et al that sonographically evaluated the subarachnoid space in 40 children (six girls and 34 boys) 0 to 3 months of age before and after an IV fluid bolus.[1] The study was a convenience sample of 40 children who were undergoing sonographic evaluation for pyloric stenosis. According to the authors, eight (20 percent) children were mildly dehydrated, and 32 (80 percent) were moderately dehydrated. It's important to note that this study did not include performance of LPs but rather assessed changes in the subarachnoid space near the location of an LP that might increase the likelihood of a successful LP. The average age of the patients was 37.1 days, and the subarachnoid space was evaluated before an IV fluid bolus and approximately one hour after the bolus. The mean IV fluid bolus volume was 22 mL/kg, with a range of 20–60 mL/kg.

The authors found that the mean size of the subarachnoid space was not significantly different between the two time periods and was 37.8 mm2 before and 36.9 mm2 one hour after bolus administration (P=0.42). Although there are a number of limitations to this study and we are unable to translate this to LP success, it would suggest that an IV fluid bolus does not change the size of the subarachnoid space at the level that an LP might be performed.

Summary

There is limited data on this topic, and a single study found no significant difference between subarachnoid space size before and after an IV fluid bolus in a small group of children 0 to 3 months of age.

Reference

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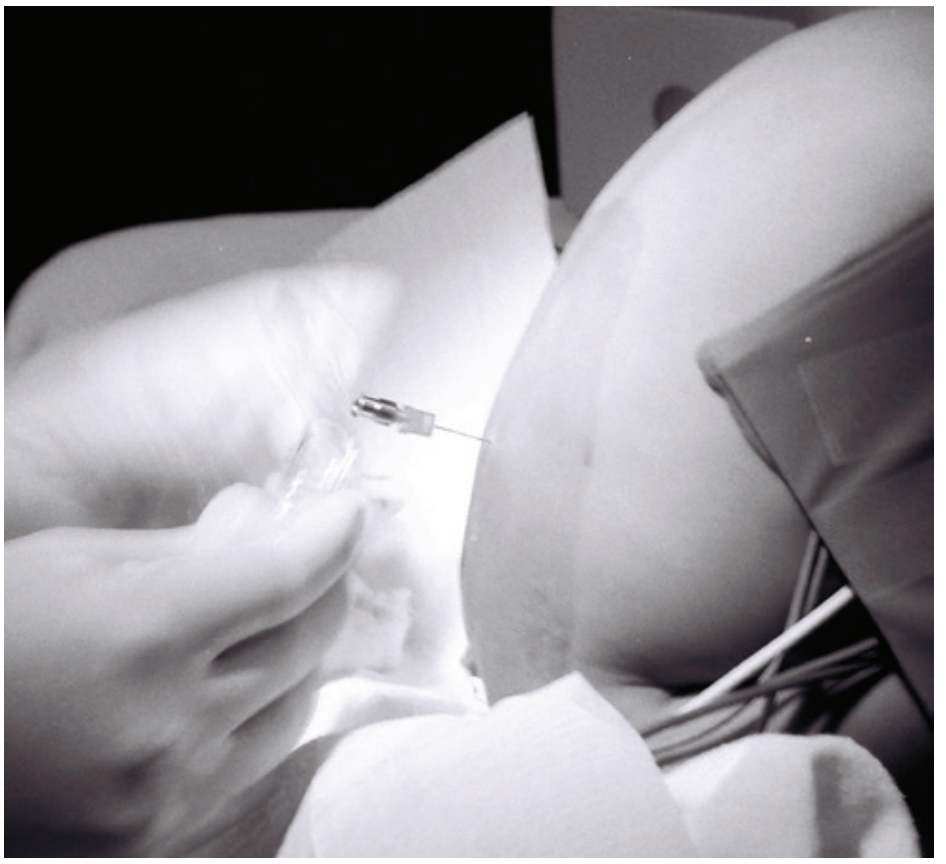

ELSBURGH CLARKE

Powerful Probiotics?

Question 2: For cases of watery diarrhea, do probiotics affect outcome?

Do you recommend the addition of probiotics to families of children with watery diarrhea? Could something this simple actually make a difference?

A 2010 Cochrane systematic review and meta-analysis by Allen et al demonstrated that the addition of probiotics decreased the mean duration of diarrhea by one day (24.76 hours [95% CI; 33.61–15.91]).[1] The meta-analysis portion included 35 trials with a total of 4,555 patients. With the addition of probiotics, there were fewer patients experiencing diarrhea lasting four days or more (29 studies with 2,853 total patients, risk ratio 0.41 [95% CI; 0.32–0.53]), and the decrease in frequency of diarrheal stools was present on day two of probiotic therapy (20 studies with 2,751 totals patients, mean difference 0.80 [95% CI; 0.45–1.14]).

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Of note, this study included both inpatient and outpatient populations. The specific probiotic dosages varied by study, but overall, the beneficial probiotic species were *Lactobacillus casei* strain GG (commonly referred to as *Lactobacillus rhamnosus* GG, labeled "LGG" on probiotic packages); *Enterococcus* lactic acid bacteria (LAB), not to be confused with the *Enterococcus faecalis* or *faecium* species we associate with disease; and *Saccharomyces boulardii*, which is actually a yeast. In summary, probiotics shortened the total duration of diarrhea and improved symptoms earlier in the course. It is also important to note that the authors were unable to find any serious adverse effects of probiotic usage.

Another separate meta-analysis by Szajewska et al specifically looked at LGG in 11 randomized controlled trials (2,444 total pediatric patients) in cases of acute gastroenteritis and found that, like in the Cochrane review, diarrhea duration decreased by about one day (1.05 days [95% CI; 0.4–1.7]).[2]

More recent randomized controlled trials have looked at specific bacterial strains and their effects on diarrhea duration. *Lactobacillus reuteri* appears to be helpful. Studies of this strain include both inpatient and outpatient settings. Dinleyici et al evaluated *Lactobacillus reuteri* in an outpatient setting (n=60 children) and found a significantly shorter diarrhea duration of 15 hours.[3] In a multicenter, randomized, single-blind clinical trial (n=127 patients) in the inpatient pediatric setting, Dinleyici et al found that treatment with *Lactobacillus reuteri* decreased the mean duration of diarrhea by 33 hours (70.7 ± 26.1 versus 103.8 ± 28.4; P< 0.001) and decreased length of stay of hospitalization as well.[4]

Conversely, not all probiotic strains appear to demonstrate similar findings. A double-blind, randomized, placebo-controlled study of *Lactobacillus acidophilus* in children in Vietnam (n=300 patients) by Hong Chau et al found no significant differences when compared to placebo.[5]

Overall, many studies demonstrate a decrease in diarrhea duration and improvement in diarrhea frequency earlier in the course when probiotics are administered. Probiotics are effective, and clinicians should routinely discuss this topic with families of children with acute watery diarrhea.

Summary

Multiple probiotics have been shown to shorten the duration of watery diarrhea by about 24 hours and have demonstrated the ability to decrease the number of diarrheal stools even earlier in the course. The most commonly studied beneficial probiotic is LGG, and other beneficial strains include *Lactobacillus reuteri* and *Saccharomyces boulardii*. For families of children with acute infectious watery diarrhea, probiotics should be routinely discussed as a potential means of symptom improvement.

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A PEEK BEHIND THE CURTAIN, FROM BENCH TO BEDSIDE

DR. CHOY is director of pharmacy practice at the New York State Council of Health-system Pharmacists in Albany.

Reversing Novel Oral Anticoagulants

What you need to know about idarucizumab (Praxbind)

by MARY CHOY, PHARMD, BCGP, FASHP

Idarucizumab (Praxbind) is the first and only specific reversal agent for a novel oral anticoagulant (NOAC) approved by the US Food and Drug Administration (FDA). The FDA granted accelerated approval to Praxbind in October 2015 and provided full approval April 17, 2018. Praxbind is a humanized monoclonal antibody fragment (Fab) indicated in patients treated with dabigatran etexilate (Pradaxa) when reversal of the anticoagulant effects of dabigatran is needed for emergency surgery/urgent procedures or in the case of life-threatening or uncontrolled bleeding.[1]

Dosing

This medication is for intravenous use only. The recommended dose of Praxbind is 5 g, provided as two separate vials each containing 2.5 g/50 mL of idarucizumab.

Medication Safety

The Institute for Safe Medication Practices (ISMP) has alerted health care professionals about the risks of confusing idarucizumab with the antineoplastic drug idarubicin.[2]

Warnings and Precautions

Thromboembolic Risk: Reversing dabigatran therapy exposes patients to the thromboembolic risk of their underlying disease. Resume anticoagulant therapy as soon as medically appropriate.

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Re-elevation of coagulation parameters: In patients with elevated coagulation parameters and reappearance of clinically relevant bleeding or those requiring a second emergency surgery/urgent procedure, an additional 5 g dose of Praxbind may be considered.

Risks of serious adverse reactions in patients with hereditary fructose intolerance due to sorbitol excipient: When prescribing Praxbind to patients with hereditary fructose intolerance, the combined daily metabolic load of sorbitol/fructose from all sources, including other drugs containing sorbitol, must be considered. The recommended dose of Praxbind contains 4 g of sorbitol, and the minimum amount of sorbitol that can trigger a serious reaction is not known.

Adverse Reactions: The most frequently reported adverse reactions (≥5 percent) in patients treated with Praxbind were hypokalemia, delirium, constipation, pyrexia, and pneumonia.

Price

The cost of Praxbind intravenous solution (2.5 g/50 mL) is approximately $3,662 for a supply of 100 mL.[3] Discount cards are available.

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The DOAC Issue

The practical application

by W. RICHARD BUKATA, MD

The Case

A 75-year-old man presents to your emergency department via paramedics. His transport time was about 25 minutes. He was driving his car on the highway when he dozed off and hit a light post. There was extensive front-end damage to the car. The airbags didn't deploy because he was driving a 1963 Buick Riviera. The steering wheel was bent.

He is awake but diaphoretic, and his breathing is rapid but unlabored. He says that his lower chest hurts when he takes a deep breath. He is developing some progressive abdominal tenderness, and a lap belt sign is starting to develop.

He has a history of diabetes (type 2), coronary artery disease, hypertension, and atrial fibrillation. His head and neck exam are normal, except for some facial abrasions. There is no chest wall crepitus, and his lungs are clear. His heart rate is irregular, consistent with atrial fibrillation, which is confirmed on a monitor. His heart rate is 115, and his blood pressure is 115/70.

His medication list includes an angiotensin-converting-enzyme inhibitor and spironolactone for his blood pressure, metformin and a sodium-glucose cotransporter 2 drug for his diabetes, and a direct oral anticoagulant (DOAC).

To make matters worse, his focused assessment with sonography in trauma (FAST) exam reveals free abdominal

fluid.

You have a general surgeon on call, and transfer to another hospital is really out of the question. The nearest hospital is 45 minutes away, and it is starting to snow.

You start the IVs and give lactated Ringer's. Your surgeon is on the way.

What about the DOAC issue?

New Option for Dabigatran

Fortunately, the patient is on dabigatran (Pradaxa). Until recently, trying to reverse DOACs was hard, if not impossible. One option is fresh frozen plasma (FFP), which takes 20 minutes to defrost, has be matched to the patient's blood type, is hard to give in large volumes quickly, and isn't at all specific for dealing with DOACs of any type. Recombinant factor VII (NovoSeven) won't be effective. Factor VII is disproportionately important in the clotting cascade, but factor VII is largely related to warfarin's mechanism of action and not the DOAC's. You could also use 4-factor prothrombin complex concentrate, but this is hardly specific with regard to counteracting a direct thrombin inhibitor.

Although you've given FFP in the past, you've only given 4-factor prothrombin complex concentrate once or twice in the setting of a bleeding patient taking warfarin. You recall that there is a new drug out that specifically counters dabigatran. It is composed of monoclonal antibodies that bind to and inactivate the drug. It is made by the same company that makes dabigatran (Boehringer Ingelheim).

It seems that all of the other options are unlikely to work for this patient. Despite receiving FFP and packed red cells, this patient is still in need of immediate surgery. Your back is to the wall. Normally in situations that are not so dire, you may get away with just waiting. Dabigatran's plasma concentration peaks in 0.5–2 hours, and depending on when the DOAC was taken, it might be largely gone by the time you see a patient. The anticoagulation half-life is about 12–14 hours in older adults. Given that the drug needs to be given twice a day, maybe you'd get lucky and the accident will have occurred just before the patient's second dose of the day.

However, seeing that our patient is definitely bleeding and on the hypotensive side, do you pull the trigger? Do you ask the pharmacy for the antidote, idarucizumab (Praxbind)? You're about to give a drug that will quickly reverse this patient's DOAC (90 percent of the dabigatran will be reversed in about four hours). Is there any other option? What about tranexamic acid? This drug stops clots from lysing. Would there be any reason not to use it? It's cheap, safe, and readily available, but it's not the specific reversal agent for dabigatran. It would seem that, in this case, it may be a reasonable option.

What about the cost of these drugs? Although it is always difficult to nail down the actual cost of drugs to a hospital (due to variables such as system discounts, middle man markups, and difficulty verifying prices found on the internet), prices are hefty, except for tranexamic acid.

In a 2016 article in *Critical Pathways in Cardiology*, the wholesale acquisition price of the usual 5 mg dose of Praxbind was listed at $3,452.50 ($3,662 on Drugs.com).[1] Depending on the dose needed, NovoSeven's price can vary from $2,262 to $18,035 (Drugs.com), and GoodRx says price ranges from $2,152 to $17,620 with its discount coupon at Costco. According to Family Practice Notebook (FPNotebook.com), 4-component prothrombin complex concentrate costs $4,500, while FFP costs $250.

Rarely discussed is the responsibility of hospitals to stock drugs that are uncommonly used, very expensive, and potentially lifesaving. The shelf life of Praxbind is 24 months. Is it reasonable to anticipate that all hospitals will have a supply on hand? With about 1,200 critical-access hospitals in the country, each having 25 acute care beds or fewer, many where weather and terrain may make transfers to larger centers impractical at times, what is the legal risk of not stocking certain essential drugs?

Case Resolution and the Evolution of Anticoagulation Reversal

Your patient receives idarucizumab early during his emergency department stay, and despite a somewhat rocky course, he survives his surgery for a ruptured liver, thanks to the specific reversal agent for dabigatran and due to the good fortune that he was taking the one DOAC with a reversal agent.

In more recent developments, the first Xa DOAC reversal agent, andexanet alfa (Andexxa), was approved by the FDA in May 2018. It reverses both rivaroxaban (Xarelto) and apixaban (Eliquis), but the indications do not cover edoxaban (Savaysa) and betrixaban (Bevyxxa).

Depending on the dose of rivaroxaban or apixaban being taken, either a low-dose or high-dose regimen of andexanet alfa is advised. The *Medical Letter* indicated that the drug had very limited availability (10 hospitals had it at the time of publication), but supplies are expected to increase in early 2019.[2] The cost is $49,500 for the high dose and half that for the low dose.

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like I had shattered my reputation by giving in to my emotions in public.

I spend much of my young physician life struggling to deal with the stress and emotions surrounding our specialty. I succumbed to my emotions often during residency and my first years as an attending. Now, after years of caring for patients, I know I have become more and more disconnected, and I find difficult scenarios no longer impact me like they used to.

When I think back to a few of the horrific cases I have seen over the years, I should really be in tears daily. Instead I have compartmentalized these tragedies further and further into the recesses of my mind. I ignore how they impact me until I just cannot overcome their cumulative weight. Even the smallest tasks are intolerable and impossible until I gather myself again. When I really pause to think about it, these responses are not normal—not for me or for anyone else in health care.

Recently, there has been some recognition of the fact that posttraumatic stress disorder (PTSD) is a real possibility in health care workers, particularly those who work with critically ill or injured patients. The American Psychiatric Association describes PTSD as a condition that occurs "in people who have experienced or witnessed a traumatic event." It further explains that PTSD sufferers "may relive the event through flashbacks or nightmares; they may feel sadness, fear, or anger; and they may feel detached or estranged from other people."[1] As some of you read this, the symptoms may sound very familiar.

According to an article in the *Journal of Medical Practice Management*, the types of physicians most prone to developing PTSD are physicians who practice emergency medicine in rural areas with limited resources, who are in residency training, who are involved in malpractice litigation, and/or who are indirectly exposed to trauma.[2] There are some of us who, unfortunately, fit into many of these categories.

Recent studies revealing the prevalence of PTSD in health care workers are disconcerting. Approximately 18 percent of all nurses, 15 to 17 percent of emergency physicians, and 11.9 to 21.5 percent of emergency medicine residents meet diagnostic criteria for PTSD.[3–5] Those are frightening numbers.

Clearly, this is a real and valid concern. So what do we need to do for our colleagues with PTSD?

Developing a departmental or, better yet, institutional approach to assisting PTSD sufferers will require a change in the way we view our profession, colleagues, and the impact emergency medicine has on our lives. Recommendations need to be accepted and practiced universally. At the crux of it, recognition should be the top priority. For all levels of health care providers in our field, the evidence says our approach to address PTSD should include:[5]

- Cognitive behavioral therapy (CBT)
- Team debriefing after care of critical patients
- Mindfulness-based stress management (MBSR)
- Teaching effective methods to use meditation or mental cues to "self-relax"

Studies examining the efficacy of CBT have demonstrated that this treatment has been useful and effective for a wide range of psychological problems, particularly in mental health disorders in children.[6] However, at present, there is minimal and low-quality evidence that CBT and mental and physical relaxation reduce occupational stress more than no intervention in health care workers.[7] Many of us are not in the practice of utilizing CBT or mindfulness in our daily work and may not be aware of what these practices involve. CBT involves increasing happiness by changing the way we respond emotionally and behaviorally to certain problems. MBSR encourages a person to focus only on their immediate present, paying attention to emotions, thoughts, and somatic feelings at that given moment. It is targeted to teach an individual to calm the mind, in turn helping to cope with times of stress. With successful use of CBT and MBSR, an individual can then move on to using meditation or verbal cues to relax and regroup in times of high stress.

Team debriefing is best led by physicians or charge nurses after a critical event. This can allow the group involved to reflect on the experience. These few minutes can also be used as an opportunity to recognize team members traumatized by events and identify them for follow-up in case they require assistance.

Education of these critical methods may be accomplished by involving our psychiatry colleagues or specialists in these fields to develop learning programs geared toward emergency medicine physicians.

To those of you who have been practicing for some time, this all may sound a little "kitschy." We trained and began our careers in an era where we view outward emotion as a sign of weakness. Perhaps we see it that way because we have become hardened, disconnected, and estranged. We are no longer in touch with the normal emotions associated with the illness, trauma, and death all around us. Perhaps we should view expression of our emotions in a different light, a sign of our own humanity.

As a group, we must have a high index of suspicion for PTSD in our colleagues (see Table 1 for a list of criteria for PTSD). We need to have our leaders advocate for effective support programs for our colleagues with PTSD. We need to develop real programs for individuals with PTSD to seek help without recourse, whether it is psychiatric therapy or time off. The road to recovery for emergency physicians who suffer from PTSD requires that we finally recognize it and ensure it is not ignored.

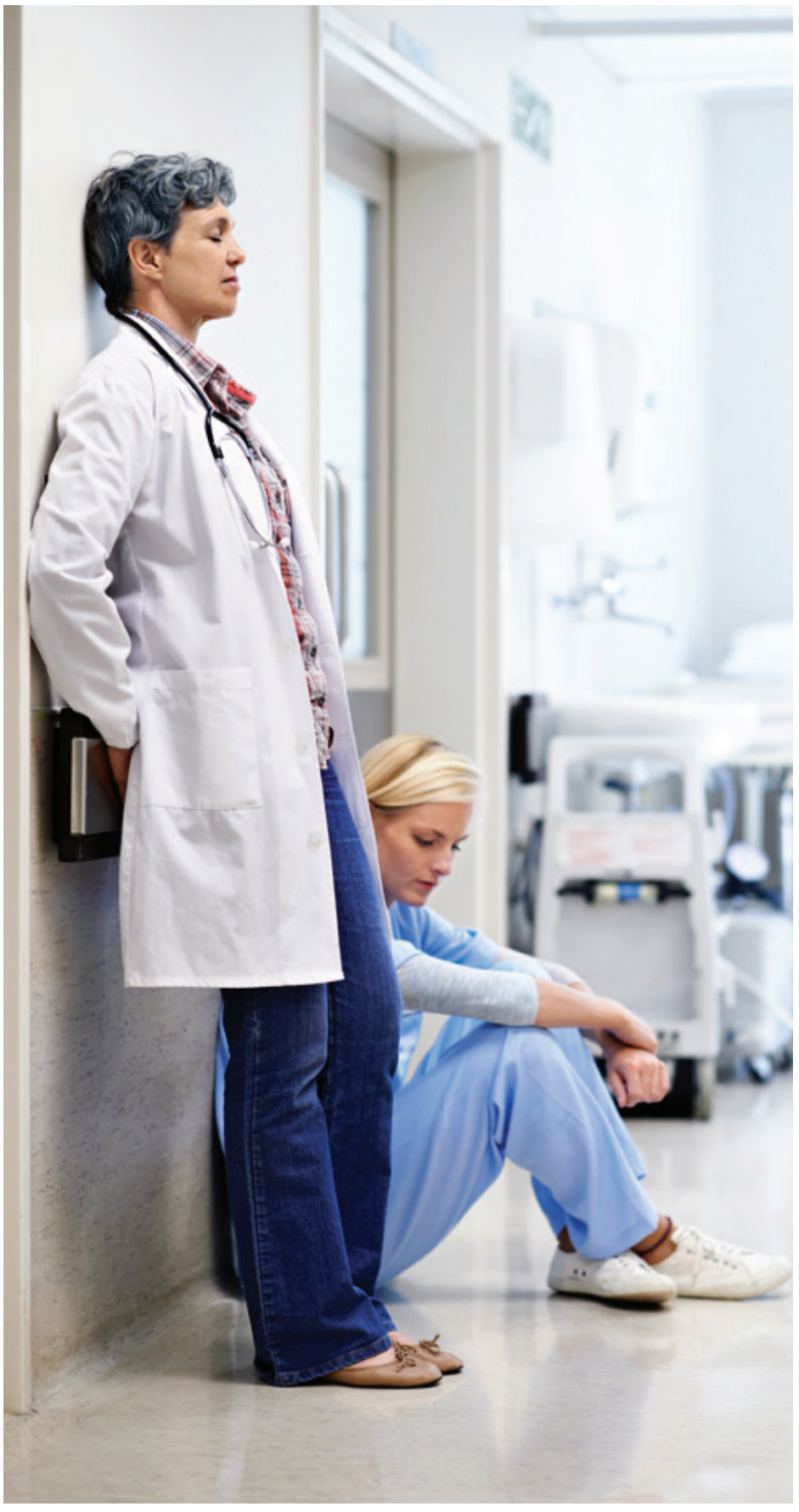

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TABLE 1: SUMMARY OF CRITERIA FOR PTSD

- Exposure to death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence
- Intrusion symptoms
- Avoidance
- Negative alterations in cognitions and mood
- Alterations in arousal and reactivity
- Duration of symptoms greater than one month
- Symptoms create distress or functional impairment
- Symptoms not due to medication, substance use, or other illness

In addition to the above criteria, the patient must have one of the following specifications:

- **Dissociative specification:** Depersonalization and/or derealization

  OR
- **Delayed specification:** Full diagnostic criteria are not met until at least six months after the trauma(s), although symptom onset may occur immediately

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MYTHS IN EMERGENCY MEDICINE

Rooted in culture, based on tradition

"What's in a name? That which we call a rose by any other name would smell as sweet."

—William Shakespeare

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by KEVIN M. KLAUER, DO, EJD, FACEP

NSAIDs and the Anti-inflammatory Myth

In the context of the opioid crisis and seeking alternatives to their use, we are perhaps relying on nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen more than ever. Coupled with the belief that we should provide "prescription-strength" pain relief (>400 mg per dose of ibuprofen), we may be increasing risk to our patients with no additional benefit. In recent years, the therapeutic ceiling of NSAIDs has been recognized and discussed. Thus, ibuprofen 400 mg per dose and 1,200 mg per day, regarded as over-the-counter doses with an excellent side effect profile, provide maximal analgesic effect.[1] At higher doses (eg, 2,400 mg per day), the risk of gastrointestinal, cardiovascular, renal, and hepatic complications is greater.[2]

So why prescribe higher doses? Many justify higher dosing by claiming the need to tap into the anti-inflammatory dosage range. Although this hypothetical benefit may be useful in chronic inflammatory conditions (eg, spondyloarthritis), most of the patients we are prescribing NSAIDs for do not have such conditions. For instance, we often presume there is an inflammatory component to most acute injuries (eg, muscle strain or joint sprain). Has anyone actually tested "inflammation" of a sprained joint? No such literature seems to be available. Furthermore, such injuries are self-limited, which begs the question, Is it the anti-inflammatory property of the NSAID that improved the patient's symptoms, or simply the analgesic effect and time?

The Research

A Cochrane database review from 2015 compared NSAIDs to other analgesics for acute soft-tissue injuries. It concluded, "There is generally low- or very low-quality but consistent evidence of no clinically important difference in analgesic efficacy between NSAIDs and other oral analgesics."[3] This review implies that if acute inflammation does exist with such injuries, either NSAIDs do not provide a clinically significant benefit in reducing inflammation or inflammation is not a significant contributor to symptoms of those injured.

Continuing with this theme are two additional Cochrane reviews. The first evaluated NSAIDs for the treatment of acute gout. One would suspect clear benefit from NSAIDs in a condition widely accepted as inflammatory in nature. After reviewing 23 trials, the authors concluded that limited evidence existed to support NSAID use for the treatment of acute gout.[4] The second reviewed the same but for spondyloarthritis. NSAIDs were efficacious based on several functional scoring tools, and there was a trend toward reduced radiographic spinal progression.[5] Thus, NSAIDs most likely provide benefit in chronic inflammatory conditions.

The concept of the anti-inflammatory effect of NSAIDs is largely a physiologic argument. If we believe NSAIDs reduce inflammation and other mechanisms of bone healing, we are forced to subscribe to the belief of some of our orthopedic colleagues that NSAIDs impede fracture healing. Many articles have been published citing these hypothetical concerns about inhibited fracture healing and studying animal models suggesting the same.

"Prostaglandins (PGs) are autocrine and paracrine lipid mediators produced by several cell types capable of mediating either a stimulatory or resorptive role depending on the physiological or pathological conditions. Administration of prostaglandins in animal models has shown to increase cortical and trabecular mass and cause hyperostosis in infants."[6]

"The activity of prostaglandins in bone tissue is defined by maintaining bone turnover balance and its reactions to humoral mediators and mechanical stress. A balanced osteoblast and osteoclast activity guarantees bone turnover equilibrium. PGE2 takes part in all processes of trauma response, including homeostasis, inflammation and healing, and plays a key role in bone physiology."[7]

However, at the end of the day, many articles have noted the lack of evidence confirming such an effect, particularly with short-term NSAID use.[8]

"What's in a name? That which we call a rose by any other name would smell as sweet."—William Shakespeare

Names do not define the subject. However, they can shape our thinking. Nonsteroidal anti-inflammatory drugs have claimed their anti-inflammatory properties merely by their name. However, the outcome benefit achieved for acutely injured patients is just as likely from their analgesic effects alone. Higher doses seem to add more risk without additional benefit.

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Opioid Use Disorder

Five steps to help you manage these patients

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

From 2002 to 2017, there has been more than a fourfold increase in the total number of opioid-related deaths, with more than a sevenfold increase in heroin overdose deaths and a 22-fold increase in synthetic opioid overdose deaths in the United States.[1] Hospital billing data from 2014 suggest that more than 90,000 emergency department patients presented with visits for unintentional, nonfatal opioid overdoses.[2] And the prevalence of suspected opioid overdose–related ED visits has significantly increased recently as well.[3]

Why does this matter to emergency physicians?

Because ED visits related to opioid use provide the perfect opportunity to start patients on treatment and kick-start their path to recovery. Many of these patients have no other access to health care, and patients are more likely to become opioid-free when treated and counseled appropriately after an opioid-related illness.

And along with the recent trends in opioid-related deaths, we've seen a parallel development in improved care of patients with the use of the partial opioid agonist buprenorphine-naloxone. This treatment modality has only recently been studied in emergency departments, and evidence suggests buprenorphine-naloxone decreases mortality, improves withdrawal symptoms, decreases drug use, improves follow-up rates, and decreases crime rates.[4–7] Therefore, it is now more important than ever that all emergency medicine providers take on the responsibility of learning about this lifesaving medication and implement it in their practices.

Recognizing Opioid Withdrawal

The clinical features of opioid withdrawal overlap with severe gastroenteritis—symptoms include crampy abdominal pain, nausea, vomiting, diarrhea, muscle aches, chills, and diaphoresis—making it easy to confuse the two. Opioid withdrawal's distinguishing features include watery eyes and nose, severe insomnia, gooseflesh, mydriasis, anxiety, restlessness, tachycardia, and hypertension.

Opioid withdrawal is rarely life-threatening. However, it may precipitate preterm labor in pregnant patients and acute coronary syndrome in patients with coronary artery disease, and there are published case reports of temporally-related Takotsubo cardiomyopathy.[8]

The various opioids feature a wide range of half-lives, ranging from a few hours with fentanyl to several days with methadone. Even after just five days of taking an opioid, physical and psychological withdrawal symptoms may develop upon cessation. Consider these five steps when prescribing opioids from the emergency department, and counsel patients appropriately (see Figure 1 for a flowchart of this process).

Step 1: Does the Patient Meet Criteria for Opioid Use Disorder?

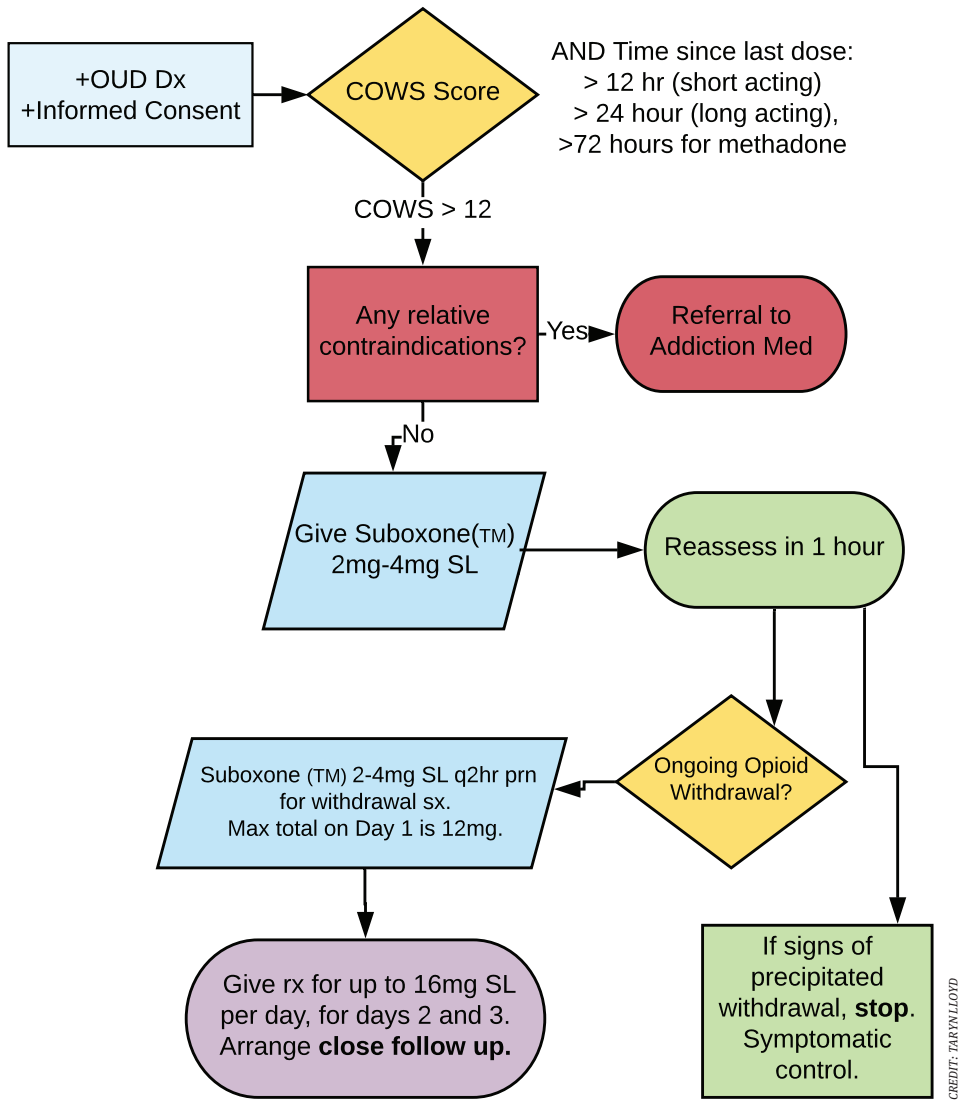
Patients must meet at least two of the following criteria in a 12-month period to meet the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5) criteria for opioid use disorder.[9]

1. Opioids are often taken in larger amounts or over a longer period than intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Opioid cravings are experienced.
5. Recurrent opioid use results in failure to fulfill major obligations at work, school, or home.
6. Continued opioid use occurs despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use occurs in situations in which it is physically hazardous.
9. Continued opioid use occurs despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Exhibits tolerance.
11. Exhibits withdrawal.

Step 2: Assess Readiness to Quit

What are the patient's goals? Are they ready and willing to start treatment in hopes of stopping their opioid use? Use the Readiness Ruler to assess the stage of change (example question: "On a scale of 1 to 10, how ready are you to make a change today?").[10] Obtain informed consent before starting buprenorphine-naloxone in the emergency department. If the patient is not ready to start the medication, share your concerns about their ongoing opioid use,

Figure 1: Assessing and Treating Opioid Withdrawal & Opioid Use Disorder



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OUD = opioid use disorder; COWS = clinical opioid withdrawal scale.

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the risk of overdose and medical complications, and harm-reduction techniques (eg, a naloxone kit, clean needles, etc.).

Step 3: Assess the Severity of Opioid Withdrawal Using COWS

Use the validated assessment tool Clinical Opiate Withdrawal Scale (COWS) to determine the withdrawal severity.[11] This scale is similar to the Clinical Institute Withdrawal Assessment scale used for alcohol withdrawal and is easily administered by ED staff. Points are assigned for the signs and symptoms of withdrawal (eg, tachycardia, sweating, restlessness, enlarged pupils, bone/joint aches, runny nose/tearing, upset gastrointestinal, tremor, yawning, anxiety/irritability, and gooseflesh). A score of 5–12 = mild, 13–24 = moderate, 25–36 = moderately severe, and greater than 36 = severe.

Patients must score at least in the moderate range to be eligible for buprenorphine-naloxone therapy.

Step 4: Buprenorphine-Naloxone and Withdrawal Symptom Treatment

Relative contraindications to buprenorphine-naloxone initiation include allergy to either buprenorphine or naloxone, hepatic dysfunction, current respiratory distress, decreased level of awareness currently, concurrent active alcohol use disorder, and concurrent benzodiazepine use.

Suboxone is buprenorphine and naloxone in a sublingual tablet. Naloxone is not active unless injected; it is a taper-resistance medication. Buprenorphine is a partial agonist that acts on the opioid mu receptor. It has a high binding affinity but only partial intrinsic activity on the receptor. This means it is effective for pain and withdrawal but features less risk of respiratory depression and side effects than pure opioids.

Step 5: Counsel and Arrange Appropriate Follow-up

Screening, Brief Intervention and Referral to Treatment (SBIRT) is a valuable tool to start patients on the path to recovery. In one study, 37 to 45 percent of patients who underwent SBIRT in the emergency department engaged with treatment at 30 days.[12] Ask for permission to discuss substance use and overdose, discuss goals, and express your concerns with their current use. Screen for other substance use.

Screen for safety as well. The opioid overdose could represent a suicide attempt. Assess the patient's goals and stage of change. Offer referral to resources in the community or hospital, based around goals (eg, housing, detox, addiction medicine clinic, family doctor services, safe injection facilities, etc.). Discuss and offer naloxone kits and clean injection supplies. Counsel patients around the high risk of accidental overdose given withdrawal and/or decrease in tolerance.

Finally, arrange rapid follow-up in an

CONTINUED *on page 26*

addiction medicine clinic or similar community clinic in one to two days if possible. Provide a prescription for daily observed dosing at a pharmacy at the appropriate dose up to 16 mg SL per day until follow-up.

All patients are more than their addiction. We have a significant opportunity to improve the lives of patients with opioid use disorders in the long run.

Special thanks to Dr. Aaron Orkin, Dr. Michelle Klaiman, and Dr. Kathryn Dong for their contributions to the EM Cases podcast that inspired this article and to Dr. Taryn Lloyd for the creation of the opioid withdrawal management algorithm diagram used in this article.

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The Department of Emergency Medicine at East Carolina University Brody School of Medicine seeks BC/BP emergency physicians and pediatric emergency physicians for tenure or clinical track positions at the rank of assistant professor or above, depending on qualifications. We continue to expand our faculty to meet the clinical needs of our patients and the educational needs of our learners. We envision further program development in clinical education, emergency ultrasound, EM-critical care, pediatric EM, and clinical research. Our current faculty possesses diverse interests and expertise leading to extensive state and national-level involvement. The emergency medicine residency includes 12 EM and 2 EM/IM residents per year. We treat more than 130,000 patients per year in a state-of-the-art ED at Vidant Medical Center. VMC is a 960+ bed level 1 trauma center and regional referral center for cardiac, stroke, and pediatric care. Our tertiary care catchment area includes more than 1.5 million people in eastern North Carolina. Additionally, we provide clinical coverage at two community hospitals within our health system. We are responsible for medical direction of East Care, our integrated mobile critical care and air medical service, and multiple county EMS systems. Our exceptional children's ED opened in July 2012 and serves approximately 25,000 children per year. Greenville, NC is a university community offering a pleasant lifestyle and excellent cultural and recreational opportunities. Beautiful North Carolina beaches are nearby. Compensation is competitive and commensurate with qualifications; excellent fringe benefits are provided. Successful applicants will be board certified or prepared in Emergency Medicine or Pediatric Emergency Medicine. They will possess outstanding clinical and teaching skills and qualify for appropriate privileges from ECU Physicians and VMC.

Confidential inquiry may be made to:
Theodore Delbridge, MD, MPH
Chair, Department of Emergency Medicine
delbridget@ecu.edu

ECU is an EEO/AA employer and accommodates individuals with disabilities. Applicants must comply with the Immigration Reform and Control Act. Proper documentation of identity and employability required at the time of employment. Current references must be provided upon request.

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Eastern Maine Medical Center has emergency medicine physician opportunities throughout Maine with flexible schedules and exceptional work/life balance.
Opportunities are available for BC/BE physicians in Bangor, Ellsworth, Blue Hill and Waterville!

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¨ In-house collaborative hospitalist service, radiology and Night Hawk Services
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¨ Trauma Service: on-call consult
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Highly desirable, family-centeredcommunities throughout Maine! Year-round access to Maine's unmatched coastline, mountains and lakes; limitless outdoor recreation opportunities and unspoiled natural beauty!

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Contact: Jamie L. Grant, Provider Recruiter, Email: providerjobs@emhs.

Baylor College of Medicine

THE DEPARTMENT OF EMERGENCY MEDICINE

Service. Education. Leadership

Exciting Emergency Medicine Opportunities

Program Director Opening

The Department of Emergency Medicine at Baylor College of Medicine is looking for outstanding applicants for the position of **Program Director**. Applicants should have a strong background in medical education with a career path directed towards graduate medical education. We are seeking an applicant with at least three years of experience per the ACGME guidelines and who embodies our values of service, education, leadership, and diversity.

The Department of Emergency Medicine at Baylor College of Medicine, a top medical school, is located in the world's largest medical center, in Houston, Texas. The Baylor Emergency Medicine Residency was established in 2010, and we recently received department status in Jan 2017. Our residency program has grown to 14 residents per year in a 3-year format. We offer a highly competitive academic salary and benefits commiserate to academic level and experience.

Our academic program is based out of Ben Taub General Hospital and Baylor St. Luke's Medical Center. Ben Taub General Hospital is the largest Level 1 trauma center in southeast Texas with certified stroke and STEMI programs that sees nearly 100,000 emergency visits per year. Baylor St. Luke's Medical Center is home to the Texas Heart Institute and with freestanding Baylor St. Luke's Emergency Centers offers multiple additional practice sites for Baylor faculty. BCM has a collaborative affiliation with eight world-class hospitals and clinics in the Texas Medical Center. These affiliations, along with the medical school's preeminence in education and research, help to create one of the strongest emergency medicine experiences in the country.

Those interested in a position or further information may contact Dr. Tyson Pillow via email pillow@bcm.edu or by phone at 713-873-7045. Please send a CV and cover letter with your past experience and interests.

LOS ANGELES CALIFORNIA

DOWNTOWN LOS ANGELES:
Quality STEM Stroke Center, good Metrics, paramedic receiving (no peds inpatients). Physician coverage 38-40hrs/day with NP & PA 12 hrs/day. 1.9 pts/hr, core group physicians average 20 years tenure. Require Board certified or Board eligible (residency trained) with experience.
Day & night shifts (max 5 nights/mo.). Salary competitive.

SAN FERNANDO VALLEY:
Paramedic receiving 130-bed hospital, 10-bed ER, 1500/pts mo. with NP & PA coverage and overlapping doctor shifts.
Volume Incentive

HOLLYWOOD URGENT CARE:
No paramedic runs

TUSTIN – ORANGE COUNTY:
Paramedic Receiving, 110-bed hospital,
9 bed ER, Anticipate 600-900 visits/mo.
Base + Incentive (patient volume + RVU) 12 hr. Shifts

LOS ANGELES:
Low volume 700/mo. urgent care non-Paramedic receiving, less stress, 20 yr. contract w/stable history. Patients 1/hr.. $260,000 - $312,000/yr + 5% Bonus.

NORWALK:
Low volume 600/mo. Paramedic receiving. Patients 8/hr. 10-year history stable. $110/hr. 24hr shifts available

Hospitalist Opportunities also available.

FAX CV to 213-482-0577
or call 213-482-0588, or email
neubauerjanice@gmail.com

Emergency Medicine & Toxicology Faculty

Rutgers Robert Wood Johnson Medical School

The Department of Emergency Medicine at Rutgers Robert Wood Johnson Medical School, one of the nation's leading comprehensive medical schools, is currently recruiting Emergency Physicians and Medical Toxicologists to join our growing academic faculty.

Robert Wood Johnson Medical School and its principal teaching affiliate, Robert Wood Johnson University Hospital, comprise New Jersey's premier academic medical center. A 580-bed, Level 1 Trauma Center and New Jersey's only Level 2 Pediatric Trauma Center, Robert Wood Johnson University Hospital has an annual ED census of greater than 90,000 visits.

The department has a well-established, three-year residency program and an Emergency Ultrasound fellowship. The department is seeking physicians who can contribute to our clinical, education and research missions.

Qualified candidates must be ABEM/ABOEM certified/eligible. Salary and benefits are competitive and commensurate with experience. Sub specialty training is desired but not necessary.

For consideration, please send a letter of intent and a curriculum vitae to:

Robert Eisenstein, MD, Chair, Department of Emergency Medicine
Rutgers Robert Wood Johnson Medical School
1 Robert Wood Johnson Place, MEB 104, New Brunswick, NJ 08901
Email: **Robert.Eisenstein@rutgers.edu**
Phone: **732-235-8717** · Fax: **732 235-7379**

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RUTGERS
Robert Wood Johnson Medical School

{ Job Opportunities }

Division Chief, Pediatric Emergency Medicine
EMS Fellowship Director/EMS Medical Director
Assistant Medical Director
PEM/EM Core Faculty
Vice Chair Research Emergency Medicine

What We're Offering:

- We'll foster your passion for patient care and cultivate a collaborative environment rich with diversity
- Salaries commensurate with qualifications
- Sign-on bonus
- Relocation assistance
- Retirement options
- Penn State University Tuition Discount
- On-campus fitness center, daycare, credit union, and so much more!

What We're Seeking:

- Experienced leaders with a passion to inspire a team
- Ability to work collaboratively within diverse academic and clinical environments
- Demonstrate a spark for innovation and research opportunities for Department
- Completion of an accredited Emergency Medicine Residency Program
- BE/BC by ABEM or ABOEM
- Observation experience is a plus

What the Area Offers:

We welcome you to a community that emulates the values Milton Hershey instilled in a town that holds his name. Located in a safe family-friendly setting, Hershey, PA, our local neighborhoods boast a reasonable cost of living whether you prefer a more suburban setting or thriving city rich in theater, arts, and culture. Known as the home of the Hershey chocolate bar, Hershey's community is rich in history and offers an abundant range of outdoor activities, arts, and diverse experiences. We're conveniently located within a short distance to major cities such as Philadelphia, Pittsburgh, NYC, Baltimore, and Washington DC.

FOR ADDITIONAL INFORMATION PLEASE CONTACT:

PennState Health

Susan B. Promes, Professor and Chair, Department of Emergency Medicine c/o Heather Peffley,
Physician Recruiter, Penn State Health Milton S. Hershey Medical Center
500 University Drive, MC A595, P O Box 855, Hershey PA 17033
Email**: hpeffley@pennstatehealth.psu.edu**
or apply online at: **hmc.pennstatehealth.org/careers/physicians**

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