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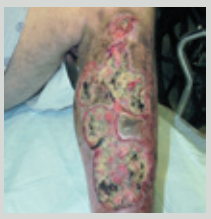

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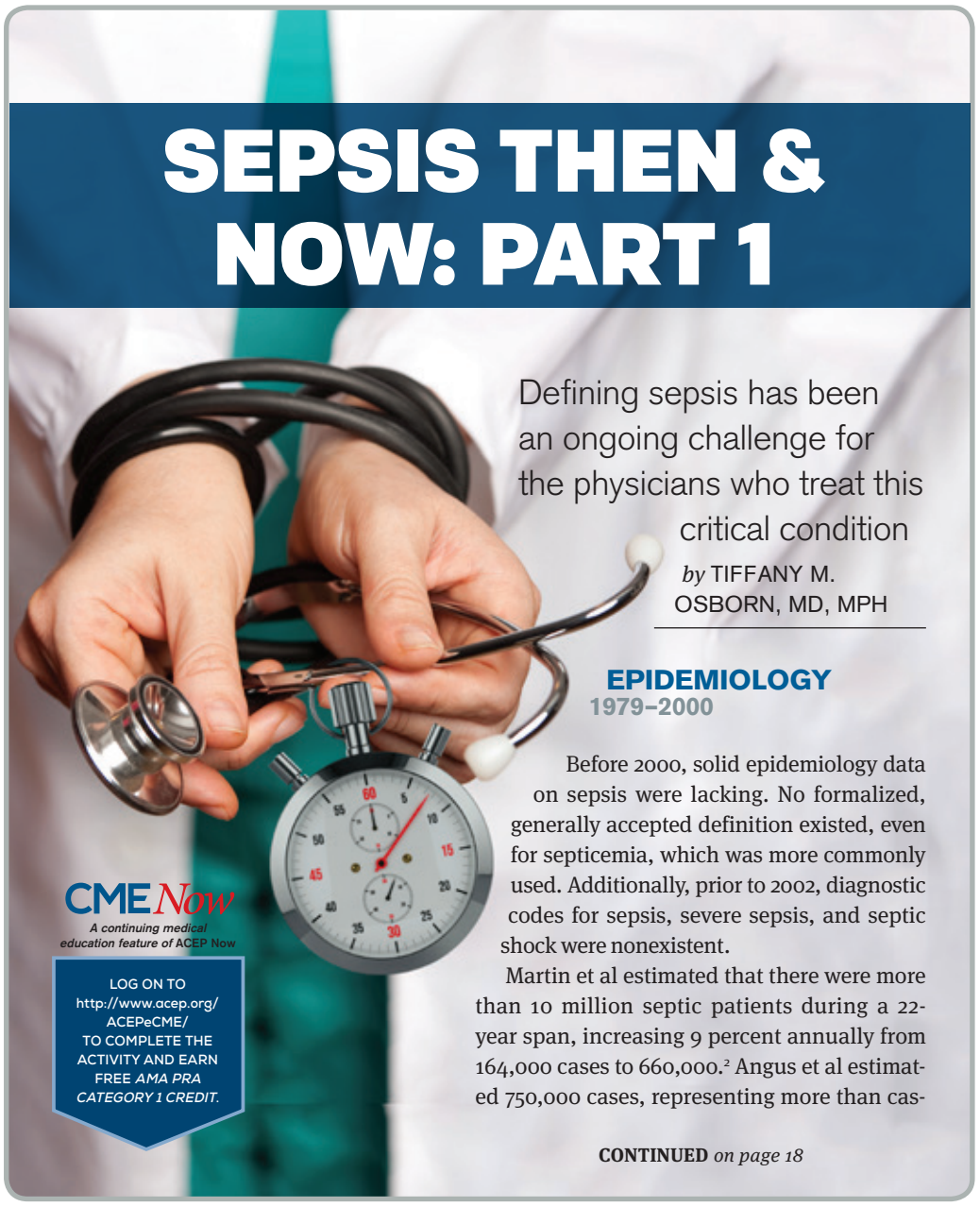

SEPSIS THEN & NOW: PART 1

Defining sepsis has been an ongoing challenge for the physicians who treat this critical condition

by TIFFANY M. OSBORN, MD, MPH

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EPIDEMIOLOGY
1979–2000

Before 2000, solid epidemiology data on sepsis were lacking. No formalized, generally accepted definition existed, even for septicemia, which was more commonly used. Additionally, prior to 2002, diagnostic codes for sepsis, severe sepsis, and septic shock were nonexistent.

Martin et al estimated that there were more than 10 million septic patients during a 22-year span, increasing 9 percent annually from 164,000 cases to 660,000.[2] Angus et al estimated 750,000 cases, representing more than cas-

CONTINUED *on page 18*

"SEIZE" THE OPPORTUNITY

Update your approach to pediatric seizures

by BORIS GARBER, DO, FACEP; AND JONATHAN GLAUSER, MD, MBA, FACEP

Seizures and epilepsy are common, serious neurologic diseases in children and adolescents.[1,2] Convulsions can be a manifestation of epilepsy or occur secondary to a complication of a systemic or central nervous system disorder. The emergency physician is usually the first provider to evaluate and stabilize children with suspected seizures. Here, we will review recent literature and share our personal experience in the approach to a seizing child in the emergency department.

Epilepsy is defined as the predisposition to generate seizures.[3,4] While generalized or focal shaking in a child readily raises a concern for seizure in caregivers and doctors alike, subtle manifestations, such as brief episodes of lip smacking in temporal lobe epilepsy or head bobbing in infantile spasms, can be challenging to correctly detect as signs of a serious neurologic disorder.

As with any other patient presenting to the emergency department, assessment of seizing children starts with determining stability and urgently addressing the ABCs.

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ETHICAL ISSUES WITH FOAM
PAGE 24

Think ELIQUIS–

For your appropriate patients with NVAF or DVT/PE

IMPORTANT SAFETY INFORMATION

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Bleeding Risk:** ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.
  - Concomitant use of drugs affecting hemostasis increases the risk of bleeding, including aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs.
  - Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.
  - The anticoagulant effect of apixaban can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). An agent to reverse the anti-factor Xa activity of apixaban is available. Please visit www.andexxa.com for more information on availability of a reversal agent.
- **Spinal/Epidural Anesthesia or Puncture:** Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

  The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic

Eliquis®
(apixaban) tablets 5mg 2.5mg

NVAF
Indicated to reduce the risk of stroke and systemic embolism in patients with NVAF[1]

DVT/PE
Indicated for the treatment of DVT and PE, and to reduce the risk of recurrent DVT and PE following initial therapy[1]

Learn more about ELIQUIS today at **hcp.eliquis.com**

DVT: deep vein thrombosis; NVAF: nonvalvular atrial fibrillation; PE: pulmonary embolism.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)
puncture occurs, delay the administration of ELIQUIS for 48 hours.

Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients.

- **Prosthetic Heart Valves:** The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients.
- **Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

ADVERSE REACTIONS
- The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS
- ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS
- **Combined P-gp and Strong CYP3A4 Inhibitors:** Inhibitors of P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) increase exposure to apixaban and increase the risk of

IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (cont'd)
bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with combined P-gp and strong CYP3A4 inhibitors.

Clarithromycin
Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

- **Combined P-gp and Strong CYP3A4 Inducers:** Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban.
- **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY CATEGORY B
- There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Reference: 1. ELIQUIS® Package Insert. Bristol-Myers Squibb Company, Princeton, NJ, and Pfizer Inc, New York, NY.

Please see Brief Summary of Full Prescribing Information, including **Boxed WARNINGS**, on adjacent pages.

Bristol-Myers Squibb Pfizer

ELIQUIS® (apixaban) tablets, for oral use

℞ ONLY

Brief Summary of Prescribing Information. For complete prescribing information consult official package insert.

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS

(B) SPINAL/EPIDURAL HEMATOMA

(A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration, Warnings and Precautions, and Clinical Studies (14.1) in full Prescribing Information]*.

(B) SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

[see Warnings and Precautions]

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary *[see Warnings and Precautions]*.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated *[see Warnings and Precautions]*.

INDICATIONS AND USAGE

Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation— ELIQUIS® (apixaban) is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery— ELIQUIS is indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery.

Treatment of Deep Vein Thrombosis—ELIQUIS is indicated for the treatment of DVT.

Treatment of Pulmonary Embolism—ELIQUIS is indicated for the treatment of PE.

Reduction in the Risk of Recurrence of DVT and PE—ELIQUIS is indicated to reduce the risk of recurrent DVT and PE following initial therapy.

DOSAGE AND ADMINISTRATION (Selected information)

Temporary Interruption for Surgery and Other Interventions

ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding *[see Warnings and Precautions]*. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be non-critical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established. (For complete *Dosage and Administration* section, see full Prescribing Information.)

CONTRAINDICATIONS

ELIQUIS is contraindicated in patients with the following conditions:

- Active pathological bleeding *[see Warnings and Precautions and Adverse Reactions]*
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions) *[see Adverse Reactions]*

WARNINGS AND PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation

Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration (2.4) and Clinical Studies (14.1) in full Prescribing Information]*.

Bleeding

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding *[see Dosage and Administration (2.1) in full Prescribing Information and Adverse Reactions]*.

Concomitant use of drugs affecting hemostasis increases the risk of bleeding. These include aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs) *[see Drug Interactions]*.

Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.

Reversal of Anticoagulant Effect

An agent to reverse the anti-factor Xa activity of apixaban is available. The pharmacodynamic effect of ELIQUIS can be expected to persist for at least 24 hours after the last dose, i.e., for about two drug half-lives. Prothrombin complex concentrate (PCC), activated prothrombin complex concentrate or recombinant factor VIIa may be considered, but have not been evaluated in clinical studies *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. When PCCs are used, monitoring for the anticoagulation effect of apixaban using a clotting test (PT, INR, or aPTT) or anti-factor Xa (FXa) activity is not useful and is not recommended. Activated oral charcoal reduces absorption of apixaban, thereby lowering apixaban plasma concentration *[see Overdosage]*.

Hemodialysis does not appear to have a substantial impact on apixaban exposure *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of apixaban. There is no experience with antifibrinolytic agents (tranexamic acid, aminocaproic acid) in individuals receiving apixaban. There is no experience with systemic hemostatics (desmopressin and aprotinin) in individuals receiving apixaban, and they are not expected to be effective as a reversal agent.

Spinal/Epidural Anesthesia or Puncture

When neuraxial anesthesia (spinal/epidural anesthesia) or spinal/epidural puncture is employed, patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

Monitor patients frequently for signs and symptoms of neurological impairment (e.g., numbness or weakness of the legs, or bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary. Prior to neuraxial intervention the physician should consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis.

Patients with Prosthetic Heart Valves

The safety and efficacy of ELIQUIS (apixaban) have not been studied in patients with prosthetic heart valves. Therefore, use of ELIQUIS is not recommended in these patients.

Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy

Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the prescribing information.

- Increased risk of thrombotic events after premature discontinuation *[see Warnings and Precautions]*
- Bleeding *[see Warnings and Precautions]*
- Spinal/epidural anesthesia or puncture *[see Warnings and Precautions]*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Reduction of Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

The safety of ELIQUIS was evaluated in the ARISTOTLE and AVERROES studies *[see Clinical Studies (14) in full Prescribing Information]*, including 11,284 patients exposed to ELIQUIS 5 mg twice daily and 602 patients exposed to ELIQUIS 2.5 mg twice daily. The duration of ELIQUIS exposure was ≥12 months for 9375 patients and ≥24 months for 3369 patients in the two studies. In ARISTOTLE, the mean duration of exposure was 89 weeks (>15,000 patient-years). In AVERROES, the mean duration of exposure was approximately 59 weeks (>3000 patient-years).

The most common reason for treatment discontinuation in both studies was for bleeding-related adverse reactions; in ARISTOTLE this occurred in 1.7% and 2.5% of patients treated with ELIQUIS and warfarin, respectively, and in AVERROES, in 1.5% and 1.3% on ELIQUIS and aspirin, respectively.

Bleeding in Patients with Nonvalvular Atrial Fibrillation in ARISTOTLE and AVERROES

Tables 1 and 2 show the number of patients experiencing major bleeding during the treatment period and the bleeding rate (percentage of subjects with at least one bleeding event per 100 patient-years) in ARISTOTLE and AVERROES.

Table 1: Bleeding Events in Patients with Nonvalvular Atrial Fibrillation in ARISTOTLE*

	ELIQUIS N=9088 n (per 100 pt-year)	Warfarin N=9052 n (per 100 pt-year)	Hazard Ratio (95% CI)	P-value
Major†	327 (2.13)	462 (3.09)	0.69 (0.60, 0.80)	<0.0001
Intracranial (ICH)‡	52 (0.33)	125 (0.82)	0.41 (0.30, 0.57)	-
Hemorrhagic stroke§	38 (0.24)	74 (0.49)	0.51 (0.34, 0.75)	-
Other ICH	15 (0.10)	51 (0.34)	0.29 (0.16, 0.51)	-
Gastrointestinal (GI)¶	128 (0.83)	141 (0.93)	0.89 (0.70, 1.14)	-
Fatal**	10 (0.06)	37 (0.24)	0.27 (0.13, 0.53)	-
Intracranial	4 (0.03)	30 (0.20)	0.13 (0.05, 0.37)	-
Non-intracranial	6 (0.04)	7 (0.05)	0.84 (0.28, 2.15)	-

* Bleeding events within each subcategory were counted once per subject, but subjects may have contributed events to multiple endpoints. Bleeding events were counted during treatment or within 2 days of stopping study treatment (on-treatment period).
† Defined as clinically overt bleeding accompanied by one or more of the following: a decrease in hemoglobin of ≥2 g/dL, a transfusion of 2 or more units of packed red blood cells, bleeding at a critical site: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal or with fatal outcome.
‡ Intracranial bleed includes intracerebral, intraventricular, subdural, and subarachnoid bleeding. Any type of hemorrhagic stroke was adjudicated and counted as an intracranial major bleed.
§ On-treatment analysis based on the safety population, compared to ITT analysis presented in Section 14.
¶ GI bleed includes upper GI, lower GI, and rectal bleeding.
** Fatal bleeding is an adjudicated death with the primary cause of death as intracranial bleeding or non-intracranial bleeding during the on-treatment period.

In ARISTOTLE, the results for major bleeding were generally consistent across most major subgroups including age, weight, $CHADS_2$ score (a scale from 0 to 6 used to estimate risk of stroke, with higher scores predicting greater risk), prior warfarin use, geographic region, and aspirin use at randomization (Figure 1). Subjects treated with apixaban with diabetes bled more (3.0% per year) than did subjects without diabetes (1.9% per year).

Table 2: Bleeding Events in Patients with Nonvalvular Atrial Fibrillation in AVERROES

	ELIQUIS (apixaban) N=2798 n (%/year)	Aspirin N=2780 n (%/year)	Hazard Ratio (95% CI)	P-value
Major	45 (1.41)	29 (0.92)	1.54 (0.96, 2.45)	0.07
Fatal	5 (0.16)	5 (0.16)	0.99 (0.23, 4.29)	-
Intracranial	11 (0.34)	11 (0.35)	0.99 (0.39, 2.51)	-

Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Other Adverse Reactions

Hypersensitivity reactions (including drug hypersensitivity, such as skin rash, and anaphylactic reactions, such as allergic edema) and syncope were reported in <1% of patients receiving ELIQUIS.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery

The safety of ELIQUIS has been evaluated in 1 Phase II and 3 Phase III studies including 5924 patients exposed to ELIQUIS 2.5 mg twice daily undergoing major orthopedic surgery of the lower limbs (elective hip replacement or elective knee replacement) treated for up to 38 days.

In total, 11% of the patients treated with ELIQUIS 2.5 mg twice daily experienced adverse reactions.

Bleeding results during the treatment period in the Phase III studies are shown in Table 3. Bleeding was assessed in each study beginning with the first dose of double-blind study drug.

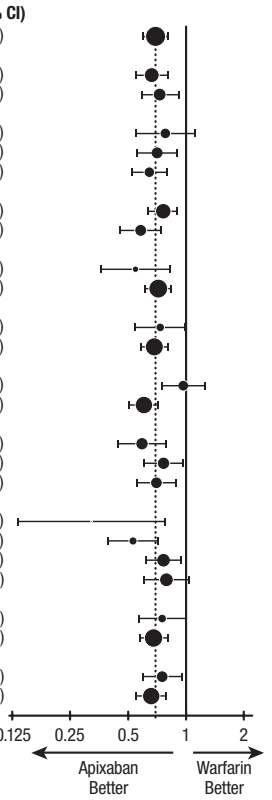
Table 3: Bleeding During the Treatment Period in Patients Undergoing Elective Hip or Knee Replacement Surgery

Bleeding Endpoint*	ADVANCE-3 Hip Replacement Surgery		ADVANCE-2 Knee Replacement Surgery		ADVANCE-1 Knee Replacement Surgery	
	ELIQUIS 2.5 mg po bid 35±3 days	Enoxaparin 40 mg sc qd 35±3 days	ELIQUIS 2.5 mg po bid 12±2 days	Enoxaparin 40 mg sc qd 12±2 days	ELIQUIS 2.5 mg po bid 12±2 days	Enoxaparin 30 mg sc q12h 12±2 days
	First dose 12 to 24 hours post surgery	First dose 9 to 15 hours prior to surgery	First dose 12 to 24 hours post surgery	First dose 9 to 15 hours prior to surgery	First dose 12 to 24 hours post surgery	First dose 12 to 24 hours post surgery
All treated	N=2673	N=2659	N=1501	N=1508	N=1596	N=1588
Major (including surgical site)	22 (0.82%)†	18 (0.68%)	9 (0.60%)‡	14 (0.93%)	11 (0.69%)	22 (1.39%)
Fatal	0	0	0	0	0	1 (0.06%)
Hgb decrease ≥2 g/dL	13 (0.49%)	10 (0.38%)	8 (0.53%)	9 (0.60%)	10 (0.63%)	16 (1.01%)
Transfusion of ≥2 units RBC	16 (0.60%)	14 (0.53%)	5 (0.33%)	9 (0.60%)	9 (0.56%)	18 (1.13%)
Bleed at critical site§	1 (0.04%)	1 (0.04%)	1 (0.07%)	2 (0.13%)	1 (0.06%)	4 (0.25%)
Major + CRNM¶	129 (4.83%)	134 (5.04%)	53 (3.53%)	72 (4.77%)	46 (2.88%)	68 (4.28%)
All	313 (11.71%)	334 (12.56%)	104 (6.93%)	126 (8.36%)	85 (5.33%)	108 (6.80%)

* All bleeding criteria included surgical site bleeding.
† Includes 13 subjects with major bleeding events that occurred before the first dose of apixaban (administered 12 to 24 hours post-surgery).
‡ Includes 5 subjects with major bleeding events that occurred before the first dose of apixaban (administered 12 to 24 hours post-surgery).
§ Intracranial, intraspinal, intraocular, pericardial, an operated joint requiring re-operation or intervention, intramuscular with compartment syndrome, or retroperitoneal. Bleeding into an operated joint requiring re-operation or intervention was present in all patients with this category of bleeding. Events and event rates include one enoxaparin-treated patient in ADVANCE-1 who also had intracranial hemorrhage.
¶ CRNM = clinically relevant nonmajor.

Figure 1: Major Bleeding Hazard Ratios by Baseline Characteristics – ARISTOTLE Study

Subgroup	n of Events / N of Patients (% per year) Apixaban	Warfarin	Hazard Ratio (95% CI)
All Patients	327 / 9088 (2.1)	462 / 9052 (3.1)	0.69 (0.60, 0.80)
Prior Warfarin/VKA Status			
Experienced (57%)	185 / 5196 (2.1)	274 / 5180 (3.2)	0.66 (0.55, 0.80)
Naive (43%)	142 / 3892 (2.2)	188 / 3872 (3.0)	0.73 (0.59, 0.91)
Age			
<65 (30%)	56 / 2723 (1.2)	72 / 2732 (1.5)	0.78 (0.55, 1.11)
≥65 and <75 (39%)	120 / 3529 (2.0)	166 / 3501 (2.8)	0.71 (0.56, 0.89)
≥75 (31%)	151 / 2836 (3.3)	224 / 2819 (5.2)	0.64 (0.52, 0.79)
Sex			
Male (65%)	225 / 5868 (2.3)	294 / 5879 (3.0)	0.76 (0.64, 0.90)
Female (35%)	102 / 3220 (1.9)	168 / 3173 (3.3)	0.58 (0.45, 0.74)
Weight			
≤60 kg (11%)	36 / 1013 (2.3)	62 / 965 (4.3)	0.55 (0.36, 0.83)
>60 kg (89%)	290 / 8043 (2.1)	398 / 8059 (3.0)	0.72 (0.62, 0.83)
Prior Stroke or TIA			
Yes (19%)	77 / 1687 (2.8)	106 / 1735 (3.9)	0.73 (0.54, 0.98)
No (81%)	250 / 7401 (2.0)	356 / 7317 (2.9)	0.68 (0.58, 0.80)
Diabetes Mellitus			
Yes (25%)	112 / 2276 (3.0)	114 / 2250 (3.1)	0.96 (0.74, 1.25)
No (75%)	215 / 6812 (1.9)	348 / 6802 (3.1)	0.60 (0.51, 0.71)
$CHADS_2$ Score			
≤1 (34%)	76 / 3093 (1.4)	126 / 3076 (2.3)	0.59 (0.44, 0.78)
2 (36%)	125 / 3246 (2.3)	163 / 3246 (3.0)	0.76 (0.60, 0.96)
≥3 (30%)	126 / 2749 (2.9)	173 / 2730 (4.1)	0.70 (0.56, 0.88)
Creatinine Clearance			
<30 mL/min (1%)	7 / 136 (3.7)	19 / 132 (11.9)	0.32 (0.13, 0.78)
30-50 mL/min (15%)	66 / 1357 (3.2)	123 / 1380 (6.0)	0.53 (0.39, 0.71)
>50-80 mL/min (42%)	157 / 3807 (2.5)	199 / 3758 (3.2)	0.76 (0.62, 0.94)
>80 mL/min (41%)	96 / 3750 (1.5)	119 / 3746 (1.8)	0.79 (0.61, 1.04)
Geographic Region			
US (19%)	83 / 1716 (2.8)	109 / 1693 (3.8)	0.75 (0.56, 1.00)
Non-US (81%)	244 / 7372 (2.0)	353 / 7359 (2.9)	0.68 (0.57, 0.80)
Aspirin at Randomization			
Yes (31%)	129 / 2846 (2.7)	164 / 2762 (3.7)	0.75 (0.60, 0.95)
No (69%)	198 / 6242 (1.9)	298 / 6290 (2.8)	0.66 (0.55, 0.79)



Note: The figure above presents effects in various subgroups, all of which are baseline characteristics and all of which were prespecified, if not the groupings. The 95% confidence limits that are shown do not take into account how many comparisons were made, nor do they reflect the effect of a particular factor after adjustment for all other factors. Apparent homogeneity or heterogeneity among groups should not be over-interpreted.

Adverse reactions occurring in ≥1% of patients undergoing hip or knee replacement surgery in the 1 Phase II study and the 3 Phase III studies are listed in Table 4.

Table 4: Adverse Reactions Occurring in ≥1% of Patients in Either Group Undergoing Hip or Knee Replacement Surgery

	ELIQUIS (apixaban), n (%) 2.5 mg po bid N=5924	Enoxaparin, n (%) 40 mg sc qd or 30 mg sc q12h N=5904
Nausea	153 (2.6)	159 (2.7)
Anemia (including postoperative and hemorrhagic anemia, and respective laboratory parameters)	153 (2.6)	178 (3.0)
Contusion	83 (1.4)	115 (1.9)
Hemorrhage (including hematoma, and vaginal and urethral hemorrhage)	67 (1.1)	81 (1.4)
Postprocedural hemorrhage (including postprocedural hematoma, wound hemorrhage, vessel puncture-site hematoma and catheter-site hemorrhage)	54 (0.9)	60 (1.0)
Transaminases increased (including alanine aminotransferase increased and alanine aminotransferase abnormal)	50 (0.8)	71 (1.2)
Aspartate aminotransferase increased	47 (0.8)	69 (1.2)
Gamma-glutamyltransferase increased	38 (0.6)	65 (1.1)

Less common adverse reactions in apixaban-treated patients undergoing hip or knee replacement surgery occurring at a frequency of ≥0.1% to <1%:

Blood and lymphatic system disorders: thrombocytopenia (including platelet count decreases)

Vascular disorders: hypotension (including procedural hypotension)

Respiratory, thoracic, and mediastinal disorders: epistaxis

Gastrointestinal disorders: gastrointestinal hemorrhage (including hematemesis and melena), hematochezia

Hepatobiliary disorders: liver function test abnormal, blood alkaline phosphatase increased, blood bilirubin increased

Renal and urinary disorders: hematuria (including respective laboratory parameters)

Injury, poisoning, and procedural complications: wound secretion, incision-site hemorrhage (including incision-site hematoma), operative hemorrhage

Less common adverse reactions in apixaban-treated patients undergoing hip or knee replacement surgery occurring at a frequency of <0.1%:

Gingival bleeding, hemoptysis, hypersensitivity, muscle hemorrhage, ocular hemorrhage (including conjunctival hemorrhage), rectal hemorrhage

Treatment of DVT and PE and Reduction in the Risk of Recurrence of DVT or PE

The safety of ELIQUIS has been evaluated in the AMPLIFY and AMPLIFY-EXT studies, including 2676 patients exposed to ELIQUIS 10 mg twice daily, 3359 patients exposed to ELIQUIS 5 mg twice daily, and 840 patients exposed to ELIQUIS 2.5 mg twice daily.

Common adverse reactions (≥1%) were gingival bleeding, epistaxis, contusion, hematuria, rectal hemorrhage, hematoma, menorrhagia, and hemoptysis.

AMPLIFY Study

The mean duration of exposure to ELIQUIS was 154 days and to enoxaparin/warfarin was 152 days in the AMPLIFY study. Adverse reactions related to bleeding occurred in 417 (15.6%) ELIQUIS-treated patients compared to 661 (24.6%) enoxaparin/warfarin-treated patients. The discontinuation rate due to bleeding events was 0.7% in the ELIQUIS-treated patients compared to 1.7% in enoxaparin/warfarin-treated patients in the AMPLIFY study.

In the AMPLIFY study, ELIQUIS was statistically superior to enoxaparin/warfarin in the primary safety endpoint of major bleeding (relative risk 0.31, 95% CI [0.17, 0.55], P-value <0.0001).

Bleeding results from the AMPLIFY study are summarized in Table 5.

Table 5: Bleeding Results in the AMPLIFY Study

	ELIQUIS N=2676 n (%)	Enoxaparin/Warfarin N=2689 n (%)	Relative Risk (95% CI)
Major	15 (0.6)	49 (1.8)	0.31 (0.17, 0.55) p<0.0001
CRNM*	103 (3.9)	215 (8.0)	
Major + CRNM	115 (4.3)	261 (9.7)	
Minor	313 (11.7)	505 (18.8)	
All	402 (15.0)	676 (25.1)	

* CRNM = clinically relevant nonmajor bleeding.
Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Adverse reactions occurring in ≥1% of patients in the AMPLIFY study are listed in Table 6.

Table 6: Adverse Reactions Occurring in ≥1% of Patients Treated for DVT and PE in the AMPLIFY Study

	ELIQUIS N=2676 n (%)	Enoxaparin/Warfarin N=2689 n (%)
Epistaxis	77 (2.9)	146 (5.4)
Contusion	49 (1.8)	97 (3.6)
Hematuria	46 (1.7)	102 (3.8)
Menorrhagia	38 (1.4)	30 (1.1)
Hematoma	35 (1.3)	76 (2.8)
Hemoptysis	32 (1.2)	31 (1.2)
Rectal hemorrhage	26 (1.0)	39 (1.5)
Gingival bleeding	26 (1.0)	50 (1.9)

AMPLIFY-EXT Study

The mean duration of exposure to ELIQUIS was approximately 330 days and to placebo was 312 days in the AMPLIFY-EXT study. Adverse reactions related to bleeding occurred in 219 (13.3%) ELIQUIS-treated patients compared to 72 (8.7%) placebo-treated patients. The discontinuation rate due to bleeding events was approximately 1% in the ELIQUIS-treated patients compared to 0.4% in those patients in the placebo group in the AMPLIFY-EXT study.

Bleeding results from the AMPLIFY-EXT study are summarized in Table 7.

Table 7: Bleeding Results in the AMPLIFY-EXT Study

	ELIQUIS (apixaban) 2.5 mg bid N=840 n (%)	ELIQUIS 5 mg bid N=811 n (%)	Placebo N=826 n (%)
Major	2 (0.2)	1 (0.1)	4 (0.5)
CRNM*	25 (3.0)	34 (4.2)	19 (2.3)
Major + CRNM	27 (3.2)	35 (4.3)	22 (2.7)
Minor	75 (8.9)	98 (12.1)	58 (7.0)
All	94 (11.2)	121 (14.9)	74 (9.0)

* CRNM = clinically relevant nonmajor bleeding.
Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Adverse reactions occurring in ≥1% of patients in the AMPLIFY-EXT study are listed in Table 8.

Table 8: Adverse Reactions Occurring in ≥1% of Patients Undergoing Extended Treatment for DVT and PE in the AMPLIFY-EXT Study

	ELIQUIS 2.5 mg bid N=840 n (%)	ELIQUIS 5 mg bid N=811 n (%)	Placebo N=826 n (%)
Epistaxis	13 (1.5)	29 (3.6)	9 (1.1)
Hematuria	12 (1.4)	17 (2.1)	9 (1.1)
Hematoma	13 (1.5)	16 (2.0)	10 (1.2)
Contusion	18 (2.1)	18 (2.2)	18 (2.2)
Gingival bleeding	12 (1.4)	9 (1.1)	3 (0.4)

Other Adverse Reactions

Less common adverse reactions in ELIQUIS-treated patients in the AMPLIFY or AMPLIFY-EXT studies occurring at a frequency of ≥0.1% to <1%:

Blood and lymphatic system disorders: hemorrhagic anemia

Gastrointestinal disorders: hematochezia, hemorrhoidal hemorrhage, gastrointestinal hemorrhage, hematemesis, melena, anal hemorrhage

Injury, poisoning, and procedural complications: wound hemorrhage, postprocedural hemorrhage, traumatic hematoma, periorbital hematoma

Musculoskeletal and connective tissue disorders: muscle hemorrhage

Reproductive system and breast disorders: vaginal hemorrhage, metrorrhagia, menometrorrhagia, genital hemorrhage

Vascular disorders: hemorrhage

Skin and subcutaneous tissue disorders: ecchymosis, skin hemorrhage, petechiae

Eye disorders: conjunctival hemorrhage, retinal hemorrhage, eye hemorrhage

Investigations: blood urine present, occult blood positive, occult blood, red blood cells urine positive

General disorders and administration-site conditions: injection-site hematoma, vessel puncture-site hematoma

DRUG INTERACTIONS

Apixaban is a substrate of both CYP3A4 and P-gp. Inhibitors of CYP3A4 and P-gp increase exposure to apixaban and increase the risk of bleeding. Inducers of CYP3A4 and P-gp decrease exposure to apixaban and increase the risk of stroke and other thromboembolic events.

Combined P-gp and Strong CYP3A4 Inhibitors

For patients receiving ELIQUIS 5 mg or 10 mg twice daily, the dose of ELIQUIS should be decreased by 50% when coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir) *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

For patients receiving ELIQUIS at a dose of 2.5 mg twice daily, avoid coadministration with combined P-gp and strong CYP3A4 inhibitors *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

Clarithromycin

Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Combined P-gp and Strong CYP3A4 Inducers

Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Anticoagulants and Antiplatelet Agents

Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding.

APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk, post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo. The rate of ISTH major bleeding was 2.8% per year with apixaban versus 0.6% per year with placebo in patients receiving single antiplatelet therapy and was 5.9% per year with apixaban versus 2.5% per year with placebo in those receiving dual antiplatelet therapy.

In ARISTOTLE, concomitant use of aspirin increased the bleeding risk on ELIQUIS from 1.8% per year to 3.4% per year and concomitant use of aspirin and warfarin increased the bleeding risk from 2.7% per year to 4.6% per year. In this clinical trial, there was limited (2.3%) use of dual antiplatelet therapy with ELIQUIS.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B

There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Treatment of pregnant rats, rabbits, and mice after implantation until the end of gestation resulted in fetal exposure to apixaban, but was not associated with increased risk for fetal malformations or toxicity. No maternal or fetal deaths were attributed to bleeding. Increased incidence of maternal bleeding was observed in mice, rats, and rabbits at maternal exposures that were 19, 4, and 1 times, respectively, the human exposure of unbound drug, based on area under plasma-concentration time curve (AUC) comparisons at the maximum recommended human dose (MRHD) of 10 mg (5 mg twice daily).

Labor and Delivery

Safety and effectiveness of ELIQUIS during labor and delivery have not been studied in clinical trials. Consider the risks of bleeding and of stroke in using ELIQUIS in this setting *[see Warnings and Precautions]*.

Treatment of pregnant rats from implantation (gestation Day 7) to weaning (lactation Day 21) with apixaban at a dose of 1000 mg/kg (about 5 times the human exposure based on unbound apixaban) did not result in death of offspring or death of mother rats during labor in association with uterine bleeding. However, increased incidence of maternal bleeding, primarily during gestation, occurred at apixaban doses of ≥25 mg/kg, a dose corresponding to ≥1.3 times the human exposure.

Nursing Mothers

It is unknown whether apixaban or its metabolites are excreted in human milk. Rats excrete apixaban in milk (12% of the maternal dose).

Women should be instructed either to discontinue breastfeeding or to discontinue ELIQUIS (apixaban) therapy, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total subjects in the ARISTOTLE and AVERROES clinical studies, >69% were 65 years of age and older, and >31% were 75 years of age and older. In the ADVANCE-1, ADVANCE-2, and ADVANCE-3 clinical studies, 50% of subjects were 65 years of age and older, while 16% were 75 years of age and older. In the AMPLIFY and AMPLIFY-EXT clinical studies, >32% of subjects were 65 years of age and older and >13% were 75 years of age and older. No clinically significant differences in safety or effectiveness were observed when comparing subjects in different age groups.

Renal Impairment

Reduction of Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

The recommended dose is 2.5 mg twice daily in patients with at least two of the following characteristics *[see Dosage and Administration (2.1) in full Prescribing Information]*:

- age greater than or equal to 80 years
- body weight less than or equal to 60 kg
- serum creatinine greater than or equal to 1.5 mg/dL

Patients with End-Stage Renal Disease on Dialysis

Clinical efficacy and safety studies with ELIQUIS did not enroll patients with end-stage renal disease (ESRD) on dialysis. In patients with ESRD maintained on intermittent hemodialysis, administration of ELIQUIS at the usually recommended dose *[see Dosage and Administration (2.1) in full Prescribing Information]* will result in concentrations of apixaban and pharmacodynamic activity similar to those observed in the ARISTOTLE study *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as was seen in ARISTOTLE.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery, and Treatment of DVT and PE and Reduction in the Risk of Recurrence of DVT and PE

No dose adjustment is recommended for patients with renal impairment, including those with ESRD on dialysis *[see Dosage and Administration (2.1) in full Prescribing Information]*. Clinical efficacy and safety studies with ELIQUIS did not enroll patients with ESRD on dialysis or patients with a CrCl <15 mL/min; therefore, dosing recommendations are based on pharmacokinetic and pharmacodynamic (anti-FXa activity) data in subjects with ESRD maintained on dialysis *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Hepatic Impairment

No dose adjustment is required in patients with mild hepatic impairment (Child-Pugh class A). Because patients with moderate hepatic impairment (Child-Pugh class B) may have intrinsic coagulation abnormalities and there is limited clinical experience with ELIQUIS in these patients, dosing recommendations cannot be provided *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. ELIQUIS is not recommended in patients with severe hepatic impairment (Child-Pugh class C) *[see Clinical Pharmacology (12.2) in full Prescribing Information]*.

OVERDOSAGE

Overdose of ELIQUIS increases the risk of bleeding *[see Warnings and Precautions]*.

In controlled clinical trials, orally administered apixaban in healthy subjects at doses up to 50 mg daily for 3 to 7 days (25 mg twice daily for 7 days or 50 mg once daily for 3 days) had no clinically relevant adverse effects.

In healthy subjects, administration of activated charcoal 2 and 6 hours after ingestion of a 20-mg dose of apixaban reduced mean apixaban AUC by 50% and 27%, respectively. Thus, administration of activated charcoal may be useful in the management of apixaban overdose or accidental ingestion. An agent to reverse the anti-factor Xa activity of apixaban is available.

PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Medication Guide).

Advise patients of the following:

- Not to discontinue ELIQUIS without talking to their physician first.
- That it might take longer than usual for bleeding to stop, and they may bruise or bleed more easily when treated with ELIQUIS. Advise patients about how to recognize bleeding or symptoms of hypovolemia and of the urgent need to report any unusual bleeding to their physician.
- To tell their physicians and dentists they are taking ELIQUIS, and/or any other product known to affect bleeding (including nonprescription products, such as aspirin or NSAIDs), before any surgery or medical or dental procedure is scheduled and before any new drug is taken.
- If the patient is having neuraxial anesthesia or spinal puncture, inform the patient to watch for signs and symptoms of spinal or epidural hematomas *[see Warnings and Precautions]*. If any of these symptoms occur, advise the patient to seek emergent medical attention.
- To tell their physicians if they are pregnant or plan to become pregnant or are breastfeeding or intend to breastfeed during treatment with ELIQUIS *[see Use in Specific Populations]*.
- How to take ELIQUIS if they cannot swallow, or require a nasogastric tube *[see Dosage and Administration (2.6) in full Prescribing Information]*.
- What to do if a dose is missed *[see Dosage and Administration (2.2) in full Prescribing Information]*.

Marketed by:
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Rev June 2018

432US1801820-04-01

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NEWS FROM THE COLLEGE

UPDATES AND ALERTS FROM ACEP

Congress Passes Comprehensive Opioid Package

On Oct. 24, President Donald Trump signed a sweeping legislative package of bills to address the nation's growing opioid epidemic. Two ED-specific provisions developed by ACEP are included that would authorize grants to expand the alternatives to opioids (ALTO) program and the ED-initiated medication-assisted treatment (MAT) program that develops best practices for providing a "warm handoff" of patients with opioid use disorder to appropriate community resources and providers to keep them engaged in addiction treatment. Throughout the many months of congressional activity on H.R. 6, ACEP worked closely with congressional leadership, House-Senate conferees, and the bill sponsors to ensure these provisions were included in the final package and used the ACEP-preferred language. During the ACEP Leadership & Advocacy Conference last May, hundreds of ACEP members advocated for these provisions with legislators and staff during their Capitol Hill visits.

Even more ACEP members in the 911 Network responding to action alerts over the past months responded to action alerts over the past months and contacted their legislators about these bills.

In other opioid-related news, ACEP participated in a meeting with White House officials, federal agencies, and other stakeholders to discuss best practices in combatting the opioid epidemic. The meeting focused on actions the Trump administration has taken to date, a review of future projects, and policies established at state and local levels that have benefited patients and reduced misuse of opioids. Particular focus was placed on National Take Back Day on Oct. 27 and how meeting participants can promote these drug-collection sites.

ACEP Releases New Information Papers

The following information papers were recently approved by the Board of Directors and published on the ACEP website:

- Advocating for a Minimum Benefit Standard Linked to the 80th Percentile of a FAIR Health-Type Usual & Customary Charge Database
- Emergency Ultrasound Standard Reporting Guidelines
- Medicaid ED Copayments: Effects on Access to Emergency Care and the Practice of Medicine

Unscheduled Procedural Sedation: A Multidisciplinary Consensus Practice Guideline

ACEP organized a multidisciplinary effort to create a clinical practice guideline specific to time-sensitive unscheduled procedural sedation, which differs in important ways from scheduled, elective procedural sedation. This guideline, which outlines the underlying background, rationale, and issues relating to staffing, practice, and quality improvement, is a resource for practitioners who perform unscheduled procedural sedation, regardless of location or patient age. Read the guidelines and FAQs at www.acep.org/by-medical-focus/procedural-sedation.

Emergency Physician Appointed to PTAC

Jennifer Wiler, MD, MBA, executive vice chair and professor in the department of emergency medicine at the University of Colorado School of Medicine in Aurora, was appointed to the Physician-Focused Payment Model Technical Advisory Committee (PTAC) on Oct. 18 by Gene L. Dodaro, U.S. comptroller general and head of the U.S. Governmental Accountability Office. Congress established the PTAC in 2015 to provide comments and recommendations to the Secretary of Health and Human Services (HHS) on physician focused payment models. Dr. Wiler's term will expire in October 2021.

ACEP Statement Opposes Public Charge Policy

In response to a new proposed rule by the U.S. Department of Homeland Security (DHS) that would make it harder for legal immigrants, who are already in the country, to obtain green cards if they've been dependent on public benefits, such as food stamps, public housing, or even Medicaid, ACEP Immediate Past President Paul Kivela, MD, MBA, FACEP, made the following statement: "ACEP joins other professional medical associations in opposing this proposed public charge rule. It is dangerous policy that, if finalized, will have negative effects for all Americans. Out of fear, when people avoid getting medical care—such as treatment for communicable diseases—it can spread and affect anyone. We urge the Trump administration to reject this immediately. ... this proposed policy will significantly affect emergency departments nationwide, because, if finalized, many in this country may delay seeking vital emergency care until they are too sick to stay away." Read the full statement at http://newsroom.acep.org/news_releases?item=122957.

ACEP Submits Comments in Response to PFS Schedule and QPP Rule

ACEP submitted a robust set of comments responding to the calendar year 2019 Medicare Part B physician fee schedule (PFS) and Quality Payment Program (QPP) proposed rule. This rule included numerous policies that impact physician payments under Medicare, most notably a proposal that would streamline documentation requirements and create a blended payment rate for office/outpatient evaluation and management (E/M) level 2 through 5 codes. However, the proposal does not initially impact the emergency medicine E/M code set. The rule also proposes a set of policies related to the third year of the QPP, the performance program established by the Medicare Access and CHIP Reauthorization Act.

CONTINUED *on page 8*

2019 Course Topics

- The ED's Role in Treating Opioid Addiction
- Coronary Risk Scores – How Good Are They?
- Sepsis – What's All the Confusion About? - Part 1
- Sepsis – What's All the Confusion About? - Part 2
- What Radiologists Say We Should/Shouldn't Order
- 2018 Stroke Guideline Controversies
- Pearls from *Risk Management Monthly*
- Pearls from *ED Leadership Monthly*
- Concussion: ED Essentials
- Serious Diseases, Outpatient Treatment - Part 1
- Serious Diseases, Outpatient Treatment - Part 2
- Pediatric Torso Trauma Assessment
- Pregnancy-Related ED Pearls
- The 2018 ATLS Guidelines – What's New?
- Pediatric Emergency Medicine Pearls - Part 1
- Pediatric Emergency Medicine Pearls - Part 2
- Clinical Consequences of ED Crowding
- Telemedicine in Emergency Care
- Latest Evidence Concerning Resuscitation Fluids
- Learning to Love High Sensitivity Troponins
- Infant Fever: Entering the Era of the Algorithm
- Toddler Fever: The Nucleotides Take Over
- Cannabinoid-Related Emergencies
- Geriatric ED Accreditation – What's it Mean?
- What's New in ED Respiratory Support?
- Pediatric Blunt Head Injury Assessment
- 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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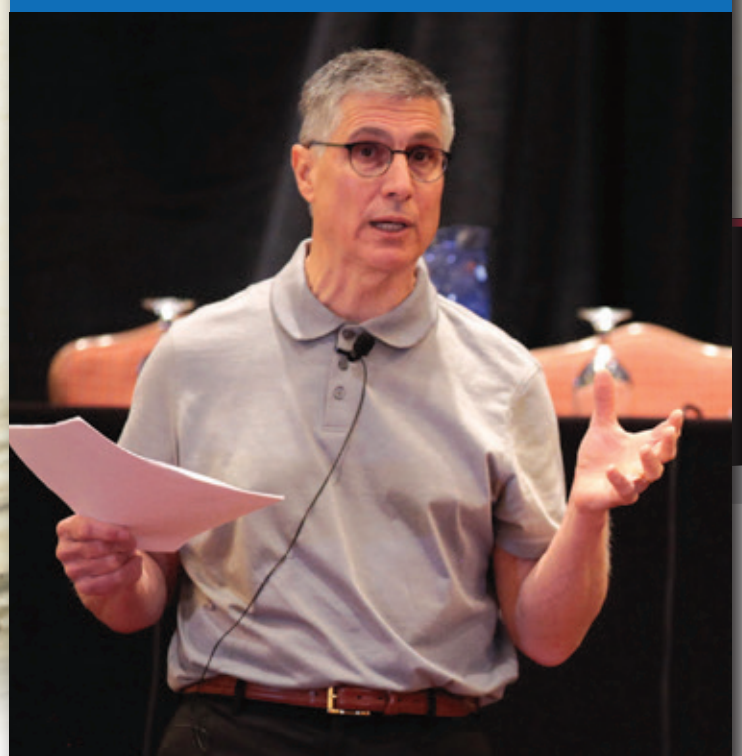

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THE BREAK ROOM

Revisiting Lactated Ringer's (LR) vs. Normal Saline (NS)

Thank you for your attention and article on the recent discussion regarding LR versus NS ["Myth: Normal Saline is the IV Fluid of Choice," April 2018]. Admittedly, I have not performed as extensive an investigation and review of the literature as you, but in my current opinion, although more evidence is forthcoming and trending in favor of LR over NS, there are four factors that merit attention and some disclosure as practice and logistics evolve.

1. Overall evidence is still modestly limited and investigated in select populations/clinical data point(s)—without necessarily incorporating other parts of care delivery (see #4).
2. Difference/benefit as well as harm may not be as pertinent and clinically relevant to the majority of ED patients.
3. Manufacturing cost difference, albeit modest, exists, and I am not sure if, additionally, hospitals charge differently for LR and NS.
4. Multiple medications, more than with NS, are not compatible for administration with LR, including some administered frequently to ED patients, including antibiotics, analgesics, hematologic agents, steroids, and ACLS/code meds.

For individual and select patients, #4 could be problematic if personnel are not sufficiently aware, and #1, #2, and #3 may not outweigh the potential benefits. With time, #1, #3, and #4 can change, but for now, when taking the specialty/entire ED population, it may not be prudent to readily discount #2 and #3.

Christopher S. Kang, MD, FACEP, FAWM
Tacoma, Washington

More Considerations When Using Buprenorphine

I am writing in response to the article "Buprenorphine Explained, And Opioid Addiction Treatment Tips" published in the June 2018 edition of *ACEP Now*.

As an emergency physician with a special interest in the identification and treatment of opioid use disorder among our patients, I was overjoyed to learn that *ACEP Now* was publishing a series of articles centered around buprenorphine and its potential as a treatment for emergency patients.

I found that this article in particular was concise yet accurate in its description of buprenorphine's pharmacology and avoided many of the common misunderstandings surrounding the drug (especially the idea that the naloxone included in Suboxone provides the opioid antagonist property).

However, I believe that it's critical to correct two misunderstandings that could result in either serious legal trouble or patient harm.

First is the implication of the statement that "...we have a medication we can give 8 mg of sublingually or 0.3 mg of subcutaneously or via IV..." which suggests that the formulation of buprenorphine administered is inconsequential. In the context of treating opioid use disorder and acute opioid withdrawal, this is incorrect, and it is illegal for a physician to prescribe or administer an opioid drug for these purposes unless that drug carries an FDA approval for the treatment of opioid use disorder.

Although there exists an increasing number of buprenorphine formulations on the market, we are limited to those that are FDA approved specifically for the treatment of addiction, such as Suboxone, Subutex, Zubsolv, Sublocade (implant), or the generics thereof when treating opioid withdrawal and dependency. It would be against federal law to administer a buprenorphine formulation that does not carry this FDA approval such as Buprenex (IM/IV) or Butrans (transdermal); even Belbuca, which is a sublingual tablet nearly identical to Subutex, is disallowed for use.

The difference between these two groups is that the latter medications are only approved for the treatment of pain, while the former carry an indication for the treatment of opioid use disorder. Unfortunately, this seeming triviality could mean risking a felony conviction for violating the Controlled Substances Act. Institutions and providers have been investigated and fined in the past for their use of injected buprenorphine to treat their patients in opioid withdrawal.

The second troublesome statement is the suggestion that, "I could give them buprenorphine...and instead of causing precipitated withdrawal, it would cause precipitated breathing." Although the author is trying to illustrate pharmacology rather than give us clinical advice, this implied clinical scenario is implausible. As described previously in the same article, buprenorphine has an extremely high affinity for the mu-receptor, higher than heroin and even higher than naloxone. You can titrate the dosage of naloxone so that it binds just enough receptors to reverse the overdose but still leaves some receptors available for agonists; this way, you create a happy median between apnea and agony.

In contrast, buprenorphine binds mu-receptors so avidly that it will come to occupy nearly all in the brain, leaving no open receptors for an agonist to bind. This creates legendarily severe precipitated withdrawal. There is no equilibrium between agonism and antagonism. As an analogy, it is the difference between walking down a staircase and jumping out the window; both reduce your altitude. However, with the first you can gradually move up or down, but once you defenestrate yourself, there's no way back up and only one destination, ground level. Naloxone also has a much shorter half-life, so the agony of its precipitated withdrawal is over in about an hour or less. The half-life of buprenorphine is anywhere from 24 to 48 hours, which ensures ongoing misery for the patient, and with its avid binding, there is no way to titrate with another agonist.

I should also mention that although buprenorphine itself is unlikely to precipitate apnea (due to the "respiratory ceiling" from its partial mu-agonism), it can cause fatal overdoses in combination with other respiratory depressants. Since we often administer naloxone to unconscious patients with no knowledge of their recent drug consumption, it would be dangerous to give buprenorphine to such patients. The patient we assume overdosed on heroin might have actually taken a few Xanax, and the buprenorphine we administer might very well push them from hypoventilation to full respiratory arrest. Not to mention that the long half-life of buprenorphine means that they will be on the ventilator while the drug is metabolized over days.

I felt it was important to clear up these implied misunderstandings since most emergency physicians are unfamiliar with buprenorphine and its applications. I hope that this serves to educate rather than frighten physicians from adopting buprenorphine in their practice, and I look forward to more coverage of emergency addiction management.

Jack C. McGeachy, MD
Tampa, Florida

NEWS FROM THE COLLEGE

CONTINUED FROM PAGE 6

ACEP

Reuben Strayer, posing with Surgeon General Dr. Jerome Adams, was ACEP's representative during a meeting about providing buprenorphine as MAT.

ACEP Participates in Buprenorphine Discussion

On Oct. 4, 2018, ACEP participated in a meeting along with 10 other provider groups to discuss with top officials of the Trump administration challenges they have had with providing buprenorphine as MAT. In attendance were the Surgeon General, Vice Adm. Jerome Adams, MD, MPH; Drug Enforcement Administration (DEA) Assistant Administrator John J. Martin; White House Office of National Drug Control Policy Acting Director James Carroll; HHS Assistant Secretary for Health Adm. Brett Giroir, MD; Assistant Secretary for Mental Health and Substance Abuse Eleanor McCance-Katz, MD, PhD; and Chief Medical Officer for the Office of the Assistant Secretary for Health, Vanila Singh, MD, MACM. ACEP member Reuben Strayer, MD, and ACEP Washington, D.C., staff participated on behalf of ACEP.

The provider groups shared the barriers they face in prescribing buprenorphine, including those brought by the X-waiver and training process; they offered suggestions for regulatory solutions. The senior administration officials were particularly interested in discussing the 72-hour rule, which allows emergency physicians to administer buprenorphine without being waivered, but requires patients to return to the emergency department for each 24-hour dosage, up to a maximum of three days. The officials concluded the meeting with commitments to examine potential regulatory approaches to add flexibility to the 72-hour rule as well as to provide DEA agents with additional training to ensure their enforcement efforts are appropriate and sensitive to patient needs.

ACEP Weighs in on Draft Legislation Regarding Out-of-Network Billing Issues

ACEP President Vidor Friedman, MD, FACEP, recently met with Sen. Bill Cassidy, MD (R-LA) and Sen. Todd Young (R-IN), two members of the Senate Bipartisan Price Transparency Workgroup, regarding their draft legislation on how to address out-of-network billing issues. The workgroup recently released a discussion draft of its legislation and requested feedback and input on how to best address this complex topic. Dr. Friedman and ACEP staff also met separately with the health staff of the senators in the workgroup for a more detailed discussion of ACEP's positions on the draft legislation. On Oct. 10, ACEP submitted a letter providing feedback on the draft bill. Read it at https://acep.org/globalassets/new-pdfs/advocacy/acep-response-on-senate-price-transparency-wg-discussion-draft-10.10.2018.pdf. ACEP's letter is part of an ongoing conversation with this bipartisan workgroup that began in March 2018.

Board Member Recognized as Health Care Influencer

Mark S. Rosenberg, DO, MBA, FACEP, has been recognized as a New Jersey health care influencer, primarily for his work in battling the opioid crisis in emergency departments. Dr. Rosenberg, along with Alexis LaPietra, DO, created the ALTO program, which helped spur an 82 percent reduction in opioid prescribing over two years.

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A NEW SPIN

MIXED COMPANY

How does gender bias affect the ED, and how do we address it?

by MARIE DELUCA, MD; CLAIRE MIN-VENDITTI, MD; MONICA SAXENA, MD, JD

It's Monday morning. You walk into a well-lit room, taking in the familiar surroundings of several colleagues in easy conversation, laughing and joking. You can't help but feel a change in the atmosphere when you are noticed. The conversation comes to a halt, and you hear someone mutter, "Now we're in mixed company."

This scene may bring to mind a woman accidentally walking into a men's locker room. In reality, this is not uncommon for women physicians in emergency medicine.

As our news feeds fill with stories of women stepping forward to call out sexual harassment and discrimination, we watch with grim recognition. Gender bias in the workplace often occurs through exploitation of gendered power dynamics, causing women to be treated differently and subsequently fall behind in systems historically built around men. At this critical juncture, we have an obligation to look within our medical community to identify and remedy sexism, from frank harassment to subtle but equally damaging unconscious bias. Marginalization and discrimination do not need to be intentional to cause harm, and in many cases, men are not even aware of the harm they cause.[1]

Emergency medicine is a male-dominated field. Although the medical field has shifted overall to near gender parity for enrolled medical students, only 27 percent of emergency physicians are women.[2,3] Evidence suggests women are also at a statistical disadvantage in emergency medicine training. A recent article found that women training in emergency medicine received inconsistent feedback on their work when compared to men. While men were consistently told how to improve clinical skills, women received conflicting advice, often centering on assertiveness and confidence.[4]

Another study found that while women and men entered emergency medicine training with similar skill sets, by the end of residency, men achieved training milestones at a higher rate than women. The achievement gap was measured as equivalent to a full three to four months of training.[5]

We must ask ourselves what sort of culture exists in our field that causes women to fall behind.

In discussions with female colleagues across several institutions, we discovered common themes. Many male doctors seem unconsciously uncomfortable working with female doctors, and the social environment of the emergency department often centers on gender norms. We hear remarks disparaging female physicians who make more money than their significant others, jokes about women's clinical judgment being clouded by feelings, and questions about whether women may be inherently less suited for the job.

Emergency medicine is not alone; gender-based exclusion has been described in other medical subspecialties and at multiple training levels.[6,7] Female medical students reported a broad range of discriminatory behaviors from male attendings, such as failing to make eye contact, employing only male pronouns when referring to physicians, and disproportionately encouraging male students compared to their female counterparts. Medical students even reported that these smaller actions disrupted learning more than blatant harassment and discrimination.[8]

Studies show gendered stereotypes adversely affect wom-

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

ACEP

Left to right: Dr. Andrea Green, Dr. Esther Choo, Dr. Sheryl Heron, Dr. Andrea Brault, and Jim Blakeman at innovatED.

Buzz About ACEP's New Diversity, Inclusion, and Health Equity Section

Dr. Andrea Green (left) and Dr. Bernard Lopez at ACEP18's innovatED.

by ANDREA GREEN, MD, FACEP

ACEP Past President Rebecca Parker, MD, FACEP, established a Diversity and Inclusion Taskforce, and Ramon W. Johnson, MD, FACEP, of the Leadership Development Advisory Group (LDAG) proposed a section focusing on diversity and inclusion. This past spring, the ACEP Board of Directors approved the Diversity, Inclusion, and Health Equity (DIHE) Section. The section focuses on leadership development, providing education on cultural competence and the different aspects of bias, and research to identify solutions for health inequities related to emergency medicine.

As the first chairperson of the DIHE Section, I was honored to lead the section through an imposing and successful inauguration during the 50th anniversary celebration at ACEP18. The section's luncheon meeting was attended by more than 85 participants. The section also hosted two educational TED Talks at innovatED: Bernard Lopez, MD, FACEP, spoke on "Implicit Bias," and Esther Choo, MD, MPH, spoke on "The Case for Dramatic Leadership in Diversity and Inclusion." The excitement, diversity, and inclusiveness of attendees at these events embody what we are about and what we will accomplish together.

DR. GREEN is chair of ACEP's DIHE Section.

en's work performance.[9,10] Repeated comments that reinforce gender stereotypes, either blatant or subtle, exert a substantial force that influences not only women's training but also their identity as doctors. One study found that female medical trainees did not feel equipped to navigate unprofessional behavior from male superiors. As a result, the women experienced guilt and resignation that this would become a part of their professional identity.[7]

Personal relationships built early in our medical careers lay the foundation for our professional trajectory. In studies of gender gaps in academic medicine, bias in the workplace is often cited as a limiting factor for career advancement.[11] If jocularity and a sense of camaraderie are restricted to our male colleagues from the start of training, this could have downstream career effects.

Even though seemingly subtle, repeated comments and acts of gender discrimination add up to a substantial force that causes women to question their legitimacy and place in medicine, affecting both their careers and their identities as women and physicians.

Let's Take Action

How do we fix this? We propose three immediate actions for leadership in our field:

1. Implement bias intervention training and discussions. Bias interventions can occur on both an individual and institution-wide scale. Attendings can incorporate their own awareness of gender bias to reduce the impact of implicit bias on resident evaluations.[12] Residency programs should incorporate data-driven implicit bias education into their lectures and grand rounds. A randomized controlled trial of bias interventions found that faculty members trained to acknowledge and actively disrupt their own bias habits were better able to promote gender equity.[13]

2. Work to increase the ratio of women faculty members and create mentorship programs for female residents. A narrative review of studies on women in academic medicine found that a lack of mentorship constitutes a significant barrier for many women who wish to pursue an academic career.[11] Seeing women in positions of leadership inspires other women and helps create an environment supportive of female physicians and trainees. Inviting female lecturers and speakers and creating mentorship and networking events for women are also structured ways for programs to support their female residents.

3. Promote and support research on gender in medicine. Research on the manifestations and impacts of gender bias in our field must be encouraged. This includes increasing support from academic journals for publication of material related to gender bias and creating platforms for sharing ideas, such as the FemInEM conference. This scholarly work ultimately benefits all of us, and academic departments should provide financial support and academic recognition equal to similar departmental administrative and academic endeavors.

All emergency physicians, both men and women, must recognize the presence of sexism within our field and take action to reduce its effects. Let's acknowledge this issue, open up dialogue, and together build a stronger, more inclusive space for us all.

ACEP
DIVERSITY INCLUSION & HEALTH EQUITY
SECTION

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DR. DELUCA (left) and **DR. MIN-VENDITTI** (right) are PGY-3 emergency medicine residents at Detroit Receiving Hospital. **DR. SAXENA** (center) is PGY-2 emergency medicine resident at John's Riverside Hospital in Yonkers, New York.

Careful attention should be given to the possibility of continuous seizure activity even if no apparent convulsions are seen. It's helpful to consider the possibility that seizures were provoked so that their causes can be diagnosed and addressed.[3] Table 1 enumerates causes of provoked seizures in patients without epilepsy.

Published guidelines on imaging in children with new-onset seizures note that in only approximately 2 to 4 percent of cases, the results altered immediate medical management.[5] While MRI is the most accurate diagnostic modality in pediatric patients, for unstable patients in whom space-occupying lesions need to be excluded, a noncontrast CT scan of brain is the modality of choice as it is rapid, is readily available, and generally does not require sedation.[5,6] It is unusual to find an acute abnormality on imaging of a normally developed child (not an infant) with a completely normal neurological examination after a brief, nonlocalizing seizure.[5] In these patients, imaging can be done on an outpatient basis as necessary. The same can be said for laboratory testing.

It is important to note that there are few studies prospectively evaluating timing of imaging in children with new-onset epilepsy. Some high- and low-risk characteristics are based on electroencephalogram (EEG) results. Most guidelines also exclude neonatal seizures.[5] A seizure in a neonate almost always requires expeditious imaging and an EEG.[6] An otherwise healthy and developmentally normal child older than 24 months after a brief first-time generalized seizure who quickly returns to normal can be discharged without medications with follow-up by pediatric neurology.[3,4,7,8] All of these patients will ultimately need an EEG, and most will require an MRI of the head.[5,6]

As in adults, most children suffering a first unprovoked seizure do not have another one, especially if their EEG is normal. The risk is higher in children with autistic spectrum disorders and if the seizure happens during sleep.[7] If it occurs, recurrent seizure is most common in the first six months after the first one.[7] While sudden unexpected death in epilepsy (SUDEP) is a known and feared entity that is currently impossible to predict in any given patient, most excess mortality in children with epilepsy is not caused by a seizure itself.[9] Great care should be taken when evaluating infants. Sepsis, meningitis, or disseminated herpes infection can manifest initially with a seizure with or without an abnormal temperature. Appropriate discharge instructions related to trauma and burn prevention, avoiding driving and taking care of babies, and not swimming or lying in a bath without close supervision are of paramount importance.

Febrile Seizures

Febrile seizures are most commonly defined as those occurring in children of defined age (6 to 60 months, per the American Academy of Pediatrics 2008 guideline) without prior afebrile seizures or neurological abnormalities and occurring in association with acute febrile illness when no other precipitating condition is identified.[10] Complex febrile seizures have focal onset, have lateralizing signs, last longer than 15 minutes, are associated with prolonged postictal deficits, or occur more than once in a given acute febrile illness. These represent approximately 40 percent of all febrile seizure presentations.[10] Febrile seizures that are not complex are defined as simple. Children typically are highly febrile if presenting soon after the seizure; low-grade fever is unusual with febrile seizures unless antipyretics were already given. Seizures lasting more than five minutes currently meet criteria for status epilepticus (SE).[11]

Management of patients with simple febrile seizures in the emergency department is similar to the management of children presenting with fever without a seizure and focuses on exclusion of serious illness such as meningitis or sepsis. The 2011 guidelines from the American Academy of Pediatrics do not recommend routine imaging, EEG, lumbar puncture, blood work, or urinalysis solely because of a simple or complex febrile seizure. Unimmunized young children (less than one year old), those on antibiotics, or those with sick appearance warrant a more extensive workup. Children seizing in the emergency department can be given benzodiazepines with intramuscular (IM), IV, intranasal, and rectal routes described.[3,10,12] The decision to prescribe rectal diazepam for use

Table 1: Select Causes of Provoked Seizures[8]

EXAMPLES	CONDITIONS	COMMENTS
Increased intracranial pressure	Meningitis, encephalitis, brain parasites and neoplasms, intracranial hematoma, idiopathic cerebral edema	National origin and travel history can point to a possibility of neurocysticercosis or malaria. Cerebral edema can occur as a complication of diabetic ketoacidosis.
Ischemic insult to brain	Ischemic stroke, anoxic brain injury	Stroke is more common in children with sickle cell disease, congenital heart disease, and acute leukemia.
Poisonings	Wide range of street drugs, various household chemicals, over-the-counter and prescription medications, and folk remedies can cause seizures in overdose or lower seizure threshold and cause susceptible patients to have a seizure	Bupropion is a commonly prescribed antidepressant that causes seizures in overdose. Organophosphate insecticides and chemical warfare agents can cause seizures in exposed individuals. Camphor-containing folk remedies can cause severe seizures. Isoniazid overdose causes seizures that respond to pyridoxine.
Metabolic derangements	Severe hyponatremia, hypoglycemia, hypo- or hypercalcemia	Infants, especially younger than 6 months, will drop their plasma sodium levels if given too much free water in their formula. Adolescents may be prone to "voluntary" water poisonings as a result of peer pressure.
Intracranial hemorrhage	Traumatic; from minimal trauma or spontaneous in coagulopathic patients; arteriovenous malformation, berry aneurysm	Possibility of nonaccidental trauma should be carefully considered. Seizure prophylaxis after traumatic brain injury is highly controversial.
Withdrawal	Neonates exposed in utero to sustained levels of opioids, sedative/hypnotics, and/or alcohol	
Febrile seizures	Typical or atypical	

Table 2: Important Diagnostic Tests for Patients in Status Epilepticus[11,13]

Consider metabolic causes; obtain bedside glucose and blood electrolytes levels (sodium, potassium, calcium, and magnesium).
Obtain cardiac rhythm strip and ECG looking for signs of toxicological emergencies.
In patients with epilepsy, ask caregivers about compliance with medications; send AED levels as appropriate.
Consider head CT, lumbar puncture, and brain MRI.
Consider IV pyridoxine if any concern for isoniazid toxicity dose, 70 mg/kg to 5,000 mg max or equal to amount of isoniazid ingested.
Consider possibility of PNES.

Table 3: Suggested Intervention Sequence in Treatment of Pediatric Status Epilepticus[3,11–14,18,19]

1. Rapidly address airway or breathing failure.
2. Administer fluid bolus for hypotension.
3. Correct any known electrolyte or glucose derangements rapidly.
4. Administer bicarbonate IV bolus for known or suspected tricyclic drug overdose.
5. Administer benzodiazepines: midazolam IM 0.1–0.2 mg/kg; lorazepam 0.1 mg/kg or diazepam 0.1-0.3 mg/kg IV push may be repeated once. Buccal and nasal routes are described for midazolam and rectal route for diazepam, but absorption may be unreliable.
6. Second-line agents are valproic acid, phenytoin or fosphenytoin, or levetiracetam. Phenobarbital can be used but would frequently require ventilatory support if given. There are case reports of lacosamide and topiramate used successfully.
7. Refractory seizure activity should prompt general anesthesia with either propofol (caution advised, especially in infants), midazolam, or barbiturates. Ketamine and intravenous magnesium have been used successfully for intractable SE. Other therapies, including ketogenic diet, hypothermia, and neurosurgery for super-refractory SE, are mostly in the pediatric ICU physician's domain.

Table 4: Select Antiepileptic Drugs (AEDs)[2,3,8,20]

While numerous new AEDs are now available, it's unknown if they are any more effective and safer than the old ones.[21] While AEDs can lower the chance of a seizure occurrence, they do not treat epilepsy or prevent the development of it.

DRUG	INDICATIONS	CONTRAINDICATIONS	COMMENTS
Phenytoin	Focal seizures, generalized tonic-clonic seizures	Not for absence or myoclonic seizures; causes blood sugar to rise	Frequent side effects
Fosphenytoin	Focal seizures, generalized tonic-clonic seizures	Same as phenytoin	Can be given IM, unlike phenytoin
Valproic acid	Broad spectrum	Severe liver disorders	
Carbamazepine	Focal seizures, generalized tonic-clonic seizures	Can exacerbate absence and myoclonic seizures	Severe and fatal dermatological reactions, especially in patients of Asian ancestry, where screening for HLA-B*1502 allele is recommended prior to treatment initiation
Ethosuximide	Absence seizures only	Any other form of epilepsy	Considered first choice for absence seizures, but in our experience is rarely prescribed by neurologists
Levetiracetam	Myoclonic, focal seizures, generalized tonic-clonic seizures		Widely used due to low incidence of side effects; unclear how effective it is
Lacosamide	Focal seizures	Caution in patients with suicidal behavior or ideation	Was not studied in children younger than 16 years
Zonisamide	Focal seizures	Cross-allergic reaction to sulfonamides	Unclear how effective it is
Perampanel	Focal seizures	Severe renal or hepatic disease	Avoid abrupt withdrawal
Oxcarbazepine	Focal seizures, generalized tonic-clonic seizures	Not for absence or myoclonic seizures	May be safer with fewer side effects than carbamazepine
Lamotrigine	Absence, focal seizures, infantile spasms, generalized tonic-clonic seizures		
Vigabatrin	Mostly for infantile spasms		Visual field defects
Phenobarbital	Myoclonic, focal seizures, generalized tonic-clonic seizures		Frequent severe side effects
Clobazam	Broad spectrum	Not recommended for first-line treatment	
Clonazepam	Broad spectrum		Difficult to use for long-term epilepsy management
Felbamate	Atonic, tonic seizures in Lennox-Gastaut syndrome	Hepatic disease	For use when other agents are ineffective
Gabapentin	Focal seizures	Not for absence or myoclonic seizures	Unclear how effective it is
Pregabalin	Focal seizures	Not for absence or myoclonic seizures	For seizures refractory to other agents only
Tiagabine	Focal seizures	Not for patients with mood disorders, suicidal ideation	Can cause seizures in patients without a seizure disorder
Rufinamide	Focal, atonic seizures in Lennox-Gastaut syndrome		
Adrenocorticotropic hormone, corticosteroids	Infantile spasms, seizures in Lennox-Gastaut syndrome		Important implications for emergency physicians in infection and shock management
Cannabinoids	Case reports for treatment of severe drug-resistant epilepsy		
Ketamine	Case reports for treatment of resistant status epilepticus		

NOTE: AEDs with US Food and Drug Administration boxed warnings are carbamazepine, felbamate, lamotrigine, perampanel, and valproic acid.

in subsequent febrile seizure episodes is controversial and must be balanced with potential of apnea after its administration.[10] As the seizure typically occurs when fever spikes, antipyretics do not help to prevent first or subsequent febrile seizures.

SE is defined as seizure activity lasting more than five minutes or recurrent seizures without recovery in between.[11,13] It is the most common neurological emergency in childhood.[13] Prolonged seizure activity can permanently damage neurons; the longer a seizure lasts, the less likely it is to stop spontaneously and the less likely it is to respond to standard antiepileptic drugs (AEDs).[3] SE appears to increase expression of drug efflux proteins in the brain, thus decreasing AED levels there.[13] As it is impossible to predict how long a given seizure will last, it's best to administer appropriate medications without delay by the fastest reliable route available and escalate therapy as necessary. Intramuscular midazolam administration has been shown to be safe and effective for prehospital SE.[12] IV access can be challenging in seizing children, especially if the veins were extensively used in the past. An intraosseous line can be lifesaving in this situation. Early cardiorespiratory monitoring and supplemental oxygen are recommended for all patients.

For suggested diagnostic workup of SE, see Table 2. For medication sequence in treating SE, refer to Table 3. Both seizure activity and medications used to terminate it can cause respiratory failure. Bag-valve-mask ventilation can sometimes stave off the need for endotracheal intubation unless emergent imaging or other diagnostic procedures are immediately needed. In case of ongoing seizure activity or altered mental status, EEG monitoring is recommended early.[11,13]

CONTINUED *on page 14*

Nonconvulsive SE (NCSE)

Prolonged brain seizure activity on EEG in a patient with altered mental status but without convulsions defines NCSE. It can present separately as an acute confusional state or develop following an observed seizure.[11] A wide variety of symptoms have been described, ranging from aphasia to severe agitation or coma.[11] It appears to have a similar incidence in children and adults and is not rare.[14,15] In settings where immediate EEG is not available, its recognition can be quite challenging. In our experience, in unclear cases, cautious administration of a weight-appropriate benzodiazepine dose can, at times, result in dramatic improvement in mental status aiding in diagnosis. Similarly to patients with convulsive SE, these patients need emergent workup focusing on diagnosing life-threatening etiologies, continuous EEG monitoring, and expeditious AED administration. As is the case with convulsive SE, the prognosis mostly depends on etiology and the degree of neurological impairment.[13]

Psychogenic Nonepileptic Seizure (PNES) and Other Seizure Mimics

PNES is defined as repeated and frequently intractable seizure activity in the absence of epileptogenic changes on concurrently recorded EEG.[16] Video EEG is necessary to firmly establish the diagnosis, and psychiatric comorbidities are common in both PNES and epilepsy.[16] As many as a quarter of children thought to be suffering from seizures are ultimately found to have PNES.[17] Misdiagnosis leads to inappropriate use of antiepileptic drugs with corresponding side effects up to and including the need for mechanical ventilation. Appropriate referral and treatment achieved an 80 percent remission rate in one study.[17]

Special Populations

There are new imaging techniques such as diffusion tensor images and MRI fused with specialized PET imaging that have improved detection of epileptogenic foci amenable to surgery in children with intractable epilepsy.[6]

Conclusion

Seizures are a common complaint in children presenting to the emergency department. The initial focus should be on stabilization of vital functions as well as rapid diagnostic workup to exclude treatable secondary causes. Febrile seizures are a unique pediatric pathology where management now mostly focuses on the concurrent, acute febrile illness. Convulsive and nonconvulsive SE are true neurological emergencies and should be stabilized as soon as possible. PNES is common, and video EEG monitoring is required to firmly establish the diagnosis.

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Suspected Non–ST-Elevation Acute Coronary Syndrome

Critical issues in the evaluation and management of these patients

by CHRISTIAN TOMASZEWSKI, MD, MS, MBA, FACEP

In June 2018, the ACEP Board of Directors approved a clinical policy on the evaluation and management of adult patients presenting with suspected non–ST-elevation acute coronary syndrome (NSTE ACS).[1] In its complete form, this policy can be found on the ACEP website at www.acep.org/patient-care/clinical-policies/nonst-elevation-acute-coronary-syndromes.

Emergency physicians routinely rule out ACS in patients presenting with chest pain and have become very good at targeting timely interventions in the obvious cases of ST-elevation myocardial infarction but still miss up to 2 percent of acute myocardial infarctions, particularly those with non–ST-elevation myocardial infarction (NSTEMI). The purpose of this policy was to focus on the initial diagnosis and treatment of patients who present with potential NSTE ACS.

In developing the policy, the ultimate outcome measure was the 30-day incidence of major adverse cardiovascular event (MACE). This includes cardiovascular death and myocardial infarction, as well as what some argue is more subjective in terms of actual need, coronary revascularization. Most emergency physicians strive to attain a miss rate of less than 1 percent. However, it is questionable if the benefits of further testing outweigh the risks of harm of untreated disease once that threshold reaches 2 percent, which the committee felt was a more realistic expectation. With shared decision making, patients may be willing to accept rates higher than those to which physicians hold themselves accountable.

Emergency departments are so often congested with patients awaiting serial testing (laboratory and noninvasive) to rule out potential ACS that entire units have been dedicated to observing these patients, yet there is questionable benefit. Researchers have been looking for diagnostic strategies, single or serial troponins, and ECGs to try to identify at-risk patients sooner and expedite their transition of care. One strategy adopted internationally and slowly taking hold in the United States is the advent of high-sensitivity troponins. Although these have great promise for detecting potential disease sooner, without proper protocols, they can lead to excessive false positives. Regardless, their use holds great promise in expediting the care of patients suspected of NSTE ACS.

Ultimately, the purpose of this policy was to help ED clinicians expedite the care of patients presenting with chest pain who are at risk for NSTE ACS. The first three questions focus on initial identification of patients at low risk for MACE, using history and limited testing. Are there patients with suspected ACS who are safe to discharge based on initial risk stratification? Do serial troponins really help, and how long do we have to wait to do that second troponin? Does getting early noninvasive diagnostic testing for ACS prior to discharge from the emergency department really help decrease MACE rates? The goal was to see if there were strategies to expedite the initial evaluation and discharge of these patients without resorting to prolonged ED stays (four to six hours or longer) while still limiting the number of 30-day MACE.

The fourth and last question looks at the role of early antiplatelet therapy in patients with acute NSTEMI and focuses on timing. Because of early literature and general consensus on the accepted use of heparin and enoxaparin, the literature search and recommendations targeted newer oral antiplatelet agents. The goal was to ensure emergency physicians were not held accountable for timely administration of such agents if such delays were not associated with worse outcomes.

For each critical question, a structured literature review was performed, evidence was systematically graded (see Table 1), and evidence-based recommendations were presented.

TABLE 1: TRANSLATION OF CLASSES OF EVIDENCE TO RECOMMENDATION LEVELS

The strength of recommendations regarding each critical question is based on the strength of evidence grading, expert opinion, and consensus discussions according to the following guidelines:

Level A Recommendations

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

Level B Recommendations

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

Level C Recommendations

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

CRITICAL QUESTIONS

1. In adult patients without evidence of ST-elevation ACS, can initial risk stratification be used to predict a low rate of 30-day MACE?

Patient Management Recommendations

- **Level A recommendations.** None specified.
- **Level B recommendations.** In adult patients without evidence of ST-elevation ACS, the history, ECG, age, risk factors, and troponin (HEART) score can be used as a clinical prediction instrument for risk stratification. A low score (≤3) predicts 30-day MACE miss rate within a range of 0 to 2 percent.
- **Level C recommendations.** In adult patients without evidence of ST-elevation ACS, other risk-stratification tools, such as thrombolysis in myocardial infarction (TIMI), can be used to predict the rate of 30-day MACE.

2. In adult patients with suspected acute NSTE ACS, can troponin testing within three hours of ED presentation be used to predict a low rate of 30-day MACE?

Patient Management Recommendations

- **Level A recommendations.** None specified.
- **Level B recommendations.** None specified.
- **Level C recommendations.**
  1. In adult patients with suspected acute NSTE ACS, conventional troponin testing at 0 and 3 hours among low-risk ACS patients (defined by HEART score 0 to 3) can predict an acceptable low rate of 30-day MACE.
  2. A single high-sensitivity troponin result below the level of detection on arrival to the emergency department or negative serial high-sensitivity troponin results at 0 and 2 hours are predictive of a low rate of 30-day MACE.
  3. In adult patients with suspected acute NSTE ACS who are determined to be low risk based on validated accelerated diagnostic pathways that include a nonischemic ECG result and negative serial high-sensitivity troponin testing results both at presentation and at 2 hours can predict a low rate of 30-day MACE allowing for an accelerated discharge pathway from the emergency department.

3. In adult patients with suspected NSTE ACS in whom acute myocardial infarction has been excluded, does further diagnostic testing (eg, provocative, stress test, computed tomography [CT] angiography) for ACS prior to discharge reduce 30-day MACE?

Patient Management Recommendations

- **Level A recommendations.** None specified.
- **Level B recommendations.** Do not routinely use further diagnostic testing (CT coronary angiography, stress testing, myocardial perfusion imaging) prior to discharge in low-risk patients in whom acute myocardial infarction has been ruled out to reduce 30-day MACE.
- **Level C recommendations.** Arrange follow-up in one to two weeks for low-risk patients in whom myocardial infarction has been ruled out. If no follow-up is available, consider further testing or observation prior to discharge (consensus).

4. Should adult patients with acute NSTEMI receive immediate antiplatelet therapy in addition to aspirin to reduce 30-day MACE?

Patient Management Recommendations

- **Level A recommendations.** None specified.
- **Level B recommendations.** None specified.
- **Level C recommendations.** P2Y12 inhibitors and glycoprotein IIb/IIIa inhibitors may be given in the emergency department or delayed until cardiac catheterization.

In conclusion, patients who present with chest pain with low risk for ACS (eg, HEART score ≤3) and a normal troponin at 0 and 3 hours post-presentation may be discharged safely, with less than a 2 percent risk of subsequent 30-day MACE. The advent of high-sensitivity troponins will help accelerate this rule-out protocol. In such low-risk cases, we could find no data to support subsequent noninvasive testing. Our ultimate goal should be to prevent harm from missing MACE, but also from overtesting patients. Finally, our last question confirms that it is acceptable to delay further antiplatelet therapy, beyond heparin, especially if there are concerns over potential adverse bleeding or competing priorities.

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SEPSIS THEN & NOW | CONTINUED FROM PAGE 1

es of breast cancer, colon cancer, and AIDS combined. With a reported 500 deaths per day, mortality for sepsis paralleled that of out-of-hospital myocardial infarction, costing $16.7 billion nationally.[3] Mortality estimates for the period ranged from 18 to 75 percent, depending on illness severity and population.[2–5] A meta-analysis reported mortality as 47 percent from 1991 to 1995 and 29 percent from 2006 to 2009, representing a 3 percent annual reduction across studies.

Most sepsis occurred external to the ICU. Approximately 60 percent of the Angus et al cases were identified outside of the ICU. In a global study, 88 percent of septic patients were identified outside of the ICU (56 percent in the emergency department, 32 percent on the ward, and 12 percent in the ICU).[6]

> "There are two great shocks for every emergency medicine resident: one, not every patient is sick, and two, many patients are much sicker than they first appear."
>
> —Peter Rosen[1]

2001–2004

Wang et al estimated that there were 571,000 suspected community-acquired severe sepsis cases presenting annually to emergency departments. Mean ED length of stay was almost five hours, with more than 20 percent of the visits lasting in excess of six hours.[7]

2009–2011

Revised estimates total 850,000 ED sepsis visits per year. This constitutes one out of every 120 ED patients. More than 70 percent of septic ED patients were admitted, with 34 percent requiring ICU admission. However, almost half had an ED length of stay of more than four hours, and more than 10 percent stayed more than eight hours.[7]

Gaieski et al demonstrated how sepsis prevalence and mortality rates change depending on the definition applied. However, what is clear is that the majority of sepsis cases are identified and initial resuscitation for them is completed outside of the ICU.[8]

> "And yet, at the present time, the subject is by no means fully elucidated, and it is not even possible to give a general definition of the term septicemia, which could currently represent all the different conceptions of its nature ... at the present time."
>
> —W.W. Van Arsdale

SEPSIS DEFINITIONS

1990s

Sepsis definitions have evolved over time (see Table 1). The 1991 American College of Chest

Physicians/Society of Critical Care Medicine conference definitions were based on a definition Bone et al decided upon when the investigators realized they needed to identify severe sepsis patients early in their course, prior to traditional culture availability, for a trial of high-dose methylprednisolone.[10,11] They defined the pragmatic, inflammatory criteria with organ dysfunction as "sepsis syndrome."[12] Despite apparent face validity, problems with applicability resulted in dissatisfaction and prompted the 1992 consensus conference.[10] Conference participants considered infection to be associated with microbial penetration and sepsis to be associated with the clinical, inflammatory response. Within this framework, the terminology of systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, and septic shock was developed. However, SIRS was criticized for lack of specificity and imperfect sensitivity.[12] Additionally, the process was criticized for predominantly involving North American representation.[13,14]

2001

The 2001 International Sepsis Definitions Conference involved five medical professional societies. A stratification system, similar to cancer staging, was developed predominantly to predict therapy response rather than predict mortality.[15] Components of the PIRO model were predisposition (baseline factors influencing survival, etc.), insult (infecting pathogens, source control, etc.), response (physiologic response, SIRS, etc.), and organ dysfunction (number of failing organs). However, the model was complex and difficult to standardize and quantify, and it was never universally applied. Both of the early definitions were based primarily on consensus of expert opinion.

2016

The Sepsis-3 definition focused primarily on infection and end-organ dysfunction. Sepsis became infection and worsening or new end-organ dysfunction based upon the Sequential Organ Failure Assessment (SOFA) scale or quick SOFA. Sepsis includes vasopressor-dependent hypotension and excludes lactate. Septic shock was defined as vasopressor-dependent hypotension with lactate elevation. The Sepsis-3 process made several important advancements. It would be the first definition conference to: 1) employ data analytics in conjunction with clinical expertise rather than solely relying on expert opinion, 2) attempt a standardized process, and 3) acknowledge continued refinement as science and our understanding evolves.[16] However, the Sepsis-3 definitions have not been universally adopted by emergency medicine, critical care, and low- and middle-income countries.[17–24] The Surviving Sepsis Campaign (SSC) ultimately decided upon an intermediate definition, where sepsis was defined by the previous severe sepsis definition (not including persistent hypotension) and septic shock remained any vasopressor-dependent hypotension. Henning et al did an excellent job illustrating implications of the different definitions.[25]

Unfortunately, sepsis continues to be an elusive entity, recognized by most and unmistakably defined by none.

DEFINITION DEVELOPMENT

Definition usefulness is based upon the purpose for which it is derived, combined with the ability to effectively operationalize it within a target environment. Purpose is based upon the context of value and prioritization.[16] Effective operationalization involves pragmatic implementation within the environment to which it is applied.

> "Emergency medicine is in the business of sensitivity."
>
> —Donald Yealy

IMPORTANCE OF PERSPECTIVE

When working in the ICU, the intensivist is concerned about specificity. There are limited resources appropriately reserved for the most acutely ill. If intensivist assessment of a patient denied ICU admission is incorrect, the patient is invariably still in a hospital-based, monitored setting. With unexpected deterioration, accommodations can be made and resources leveraged. In the emergency department, the physician is concerned about sensitivity, or who could be missed. An incorrect assessment of a patient who decompensates after being discharged home is not afforded the same accommodations and may have significant consequences. For example, when the SSC data from the septic shock manuscript were divided into hypotension and normal lactate or normotension and lactate >4 mmol/L, the mortality was essentially the same at 30 percent. Hypotension was included in the definition of sepsis, and lactate was not. Although the authors never dissuaded using lactate because, from their perspective, lactate added no additional predictive validity for mortality or ICU resources, it was only retained during hypotension. From an emergency medicine perspective, a quick point-of-care test that identifies a patient at risk is of great value. If mortality and a prolonged ICU stay are averted, it could signal a job well-done through early identification and treatment rather than unnecessary information.

If definition usefulness is based on priorities, it seems important to know what is valued the most by the clinicians who are implementing the definition.

> "Labeling already differentiated ICU patients is very different than sorting, or triaging, undifferentiated patients in the ED or on hospital wards."
>
> —David Gaieski and Munish Goyal

SURVIVING SEPSIS CAMPAIGN

ACEP's involvement with the SSC began in 2003, when an emergency physician who had just completed a critical care fellowship was in Amsterdam taking the European critical care boards at the European Society of Intensive Care Medicine annual congress, as the US boards were not an option. While there, the physician went to the SSC presentation in an auditorium filled with hundreds of intensivists and listened to the Phase II and III plans for this international critical care collaborative. During the question period, the emergency physician asked a simple inquiry: "If 50 percent of sepsis in the United States presents through the emergency department, would it be of benefit to have emergency medicine involved?"

A proposal was drafted, and conversations with the ACEP Board of Directors began through Arthur Kellermann, MD, MPH, FACEP. A lecture with panel discussion was arranged for the ACEP Scientific Assembly. In a room accommodating 200 people, approximately 25 people attended that inaugural lecture. There were no other sepsis talks at ACEP that year.

Sepsis didactics became a standing component of Scientific Assembly. An article documenting ACEP's alliance with the SSC and a letter from the ACEP president regarding ACEP's involvement were sent to 35,000 members. During this time, sepsis mortality was high, with an estimated 500 deaths per day in the United States alone. As part of Phase I, Graham Ramsay, MD, conducted a survey of more than 1,000 physicians from six countries and found fewer than 17 percent of physicians agreed on a common definition or a standard treatment. In 2003, ACEP participated with representatives from 11 international medical professional organizations in the creation of the first set of sepsis management guidelines advising a standardized management approach to sepsis. Guided by Phillip Dellinger, MD, there was meaningful collaboration. During periods of intense academic discussion, where few agreed on how specific data were interpreted, he would carefully consider the different perspectives and then skillfully find common ground. ACEP contributed meaningfully with 100 percent of the major content revisions and 75 per-

CONTINUED *on page 20*

TABLE 1: MODERN SEPSIS DEFINITIONS

YEAR	DEFINITION NAME OR IDENTIFIER	DEFINING ELEMENTS
1987	Bone, from methylprednisolone trial	• Inflammatory criteria, ≥1 organ dysfunction (AMS, hypoxemia, elevated lactate, oliguria)
1991	ACCP, SCCM Definitions Conference	• Septicemia abandoned • SIRS concept proposed but not defined • Categories of sepsis, severe sepsis, and septic shock established • MODS terminology
2001	ACCP, SCCM, ATS, ESIM, SIS	• Expanded SIRS criteria, PIRO stratification: predisposition, insult, response, organ dysfunction
2015	Centers for Medicare and Medicaid Services	• Severe sepsis: Infection* and SIRS and organ dysfunction including elevated lactate (>2 mmol/dL) • Septic shock: Severe sepsis with persistent hypotension OR lactate >4 mmol/dL
2016	Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)	• Severe sepsis abandoned • Focus on organ failure/dysfunction • **Sepsis:** organ failure focus including vasopressor-dependent hypotension • **Septic shock:** vasopressor-dependent hypotension with elevated lactate
2016	Surviving Sepsis Campaign	• **Severe sepsis:** abandoned • **Sepsis:** previous severe sepsis (lactate qualifies, no vasopressor-dependent hypotension) • **Septic shock:** previous septic shock, includes all vasopressor-dependent hypotension ± lactate

*AMS: altered mental status, SIRS: systemic inflammatory response syndrome, ACCP: American College of Chest Physicians, SCCM: Society of Critical Care Medicine, MODS: multiple organ dysfunction syndrome, ATS: American Thoracic Society, ESICM: European Society of Intensive Care Medicine, SIS: Surgical Infection Society, *Presumed or identified infection*

cent of moderate content revisions accepted. Through Phase III, headed by Mitchell Levy, MD, from the SSC, and Sean Townsend, MD, from the Institute for Healthcare Improvement (IHI), an innovative approach of structured, data-driven implementation was taken. Although there were periods of academic differences of opinion on specific elements of the guidelines, the representatives generally came to a consensus and worked collaboratively with mutual respect.

Over the past two years, simultaneous with the departure of Dr. Dellinger from the SSC, the collaborative culture changed. Although the majority of sepsis patients are identified and initially treated outside of the ICU, clinical perspectives from service lines such as emergency medicine, hospitalists, nurses, or infectious disease were not considered when developing definitions. This decision resulted in reduced uptake. Additionally, a few months after completing a yearlong process of guideline development, SSC executive committee members, independent of the multispecialty guideline committee, published the Hour-1 Bundle. This bundle, directed toward ED practice without representation from the emergency medicine community and without review by the multispecialty SSC Guidelines Committee, is misguided and should serve as an alarming precedent for all professional organizations participating in the SSC. When a letter to the editor was written in response to the Hour-1 Bundle, it was not published due to a Society of Critical Care Medicine (SCCM) policy of having concerns directed to the guideline committee chair.

This is a challenging time. ACEP is working diligently with SCCM and the SSC. Although individual service lines can incrementally impact mortality, no service line can truly optimize sepsis survival alone. From 2003 to 2015, patient survival has improved due in part to this global cooperative work. I hope we can get back to the real mission, caring for the patients we are called upon to serve. Our patients need us all to be more than individual service lines; they need us to provide a service.

Part 2 of this history will appear in the December issue.

ONLINE EXCLUSIVE

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Derm Intervention

Complaints about your leg? You may have a problem

by GINA VENTO, MD; MATTHEW ROEHRS, DO; AND DAVID EFFRON, MD, FACEP

The Case

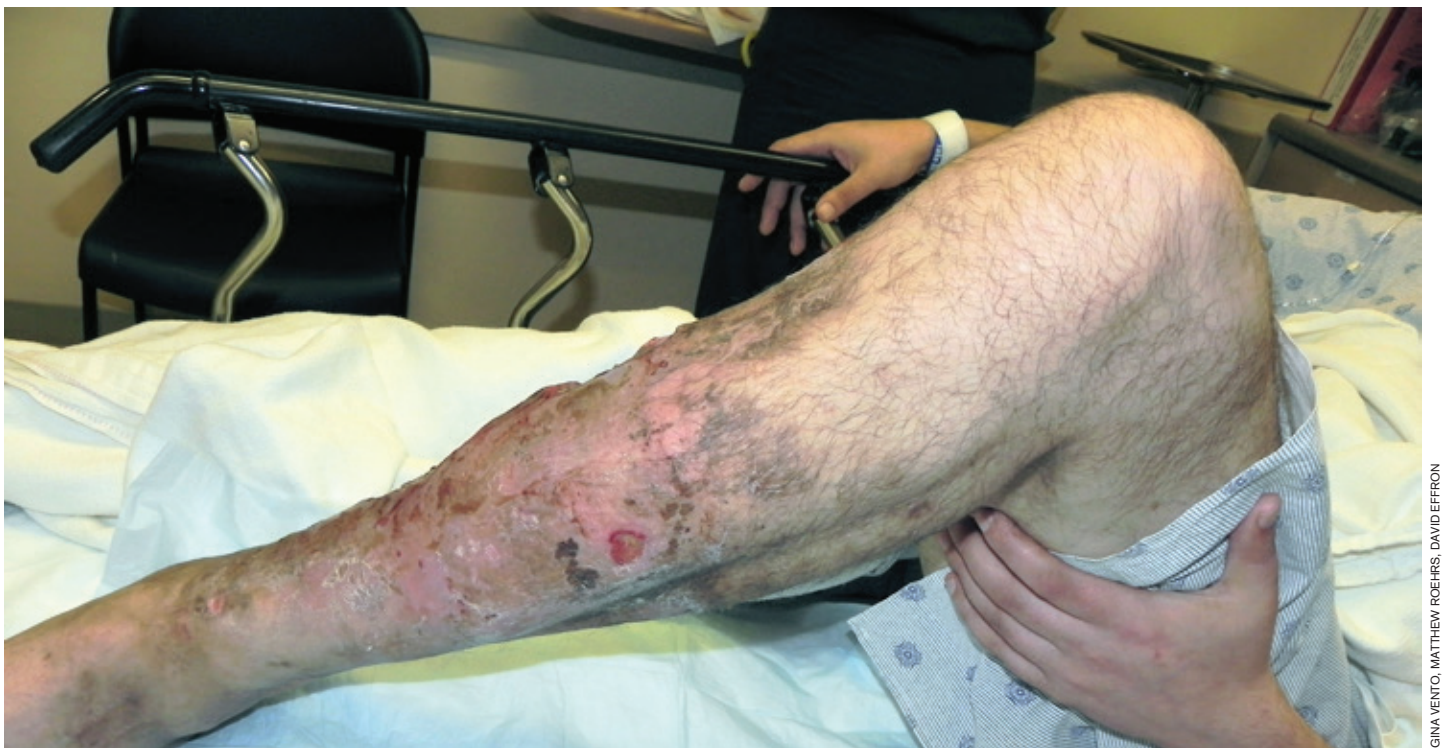
A 30-year-old man presented to the emergency department with a left leg wound that had been present for five years and "worsening over the past four months." The patient presented because he was on the verge of losing his job because of the odor from the wound. The patient described the lesion as painful, making it difficult to ambulate. He denied recent trauma to the area. However, he had a remote history of a car accident years ago but didn't remember any injury to the leg. He reported subjective fevers, nausea, and vomiting over the past few weeks. His past medical history was significant for smoking and nephrotic syndrome. No family history of autoimmune disorders was reported, and he denied any prior dermatological conditions.

Upon entering the patient's room, an intense, putrid odor was noted. The patient appeared in no acute distress, and his vital signs were normal. The patient had large ulcers with undermined borders and erythematous edges on the entire aspect of his left lateral and medial leg (see Figures 1 and 2). The leg was diffusely tender to palpation, with distal strength and sensation intact. No edema was noted. Dorsalis pedis and posterior tibial pulses were intact.

Workup for the patient included basic labs and a wound culture. Radiographs of the tibia showed a large soft tissue defect overlying the medial aspect of the proximal and mid tibia with no periosteal reaction to suggest osteomyelitis. The patient's labs were significant for a leukocytosis of 13.7, hemoglobin of 9.7, normal lactate, and renal dysfunction with a creatinine of 2.67. The patient was started on vancomycin and Zosyn (piperacillin and tazobactam) and admitted to the medicine service. Dermatology and general surgery were consulted once the patient was admitted.

Background

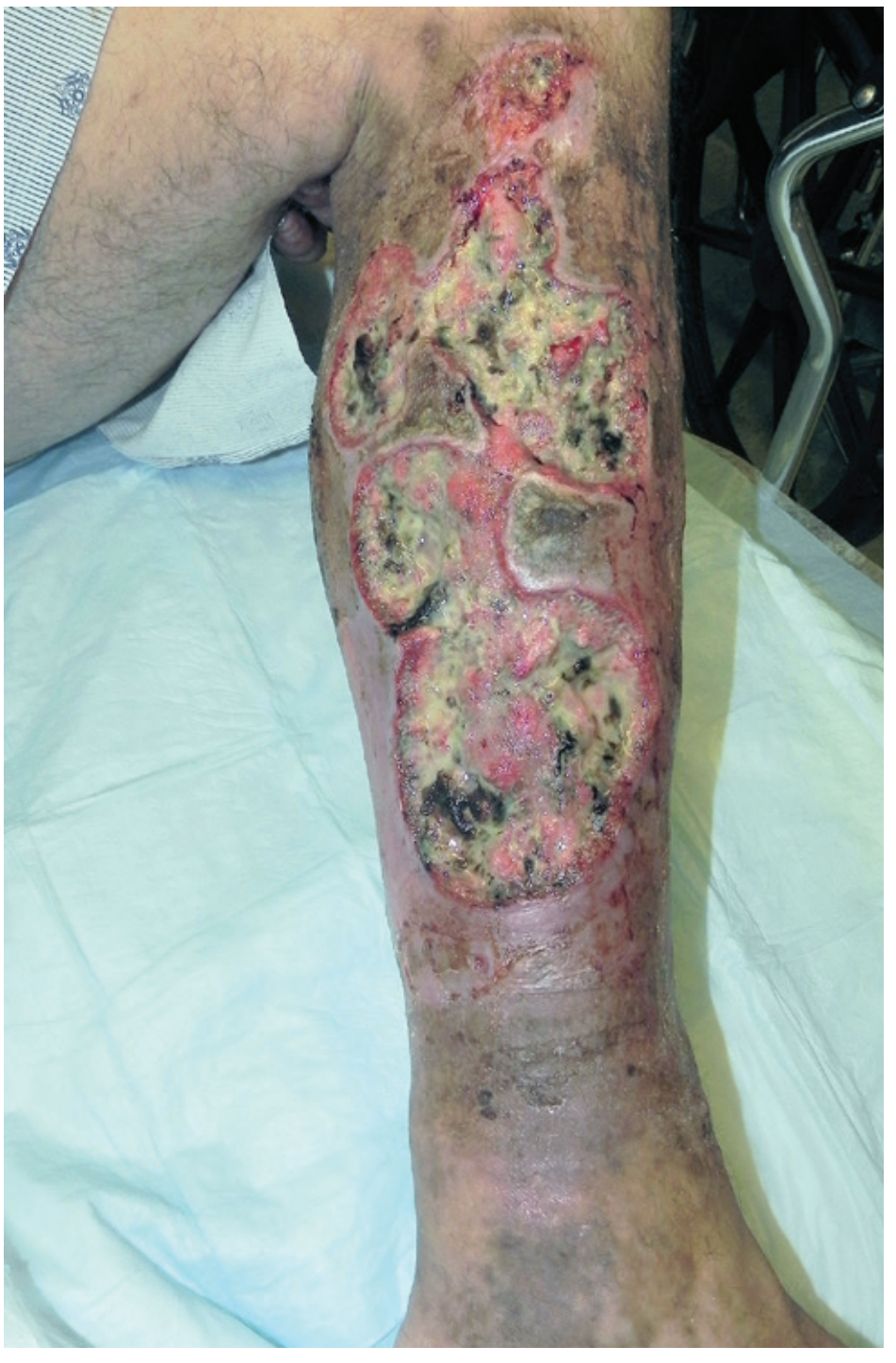
Skin complaints are common reasons for visits to the emergency department, with skin infections, such as cellulitis, being one of the most common. Differentiating toxic skin conditions from benign skin conditions is essential. This patient's condition could be concerning for a necrotizing infection, but that possibility is less likely given the time frame. Initial concern was for a chronic infection. The patient's wound cultures grew *Staph*, which could have been a contaminant versus infection. Punch biopsy revealed acute and chronic inflammation. Dermatology concluded that this presentation was consistent with pyoderma gangrenosum.



GINA VENTO, MATTHEW ROEHRS, DAVID EFFRON

FIGURE 1(ABOVE): Large ulcers with undermined borders and erythematous edges on the patient's left lateral leg.

FIGURE 2 (BELOW): Large ulcers with undermined borders and erythematous edges on the patient's left medial leg.



The incidence of pyoderma gangrenosum is estimated to be three to 10 cases per million people per year. It is often associated with systemic disease such as inflammatory bowel disease, arthropathies, and hematologic diseases. The pathogenesis is thought to be related to neutrophil dysfunction with a component related to abnormal immune system response. Treatment is dependent on the severity of the disease. Local pyoderma gangrenosum is treated with a barrier cream and wound care to try to prevent infection. Topical steroids can also be used. If the disease is more severe, systemic corticosteroid therapy should be considered. If this does not seem to be helping, cyclosporine should be considered. Systemic steroids can result in improvement in as little as one week. It is also important to address underlying systemic disease that may be contributing to the condition.

Case Resolution

This patient was discharged on prednisone 50 mg twice a day, with a plan to taper over several weeks. It was also recommended that the patient use Vaseline with Xeroform and Kerlix for dressing changes. Cyclosporine could not be considered for this patient as he had renal disease. The patient was discharged from the hospital and was told to follow up closely with dermatology. The patient did not show up for his follow-up visits and was lost to follow-up.

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RESOURCES FOR FURTHER READING

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ETHICAL ISSUES WITH FOAM

The online movement should not overlook ethical standards from traditional medical education

There is an ethical imperative for the FOAM community to establish firm safeguards, aggressively self-regulate, and promote the skepticism that is the bedrock of scientific advancement.

by NATHAN G. ALLEN, MD, FACEP; EASHWAR B. CHANDRASEKARAN, MD, MSC; REBECCA R. GOETT, MD, FACEP, FAAHPM; NICHOLAS H. KLUESNER, MD, FACEP; AND LAURA VEARRIER, MD, DBIOETHICS; ACEP ETHICS COMMITTEE

FOAM, free open access medical education, is an online movement taking place across social media, blogs, and podcasts that is challenging traditional methods of medical education.[1,2] Its acronym coined in 2012, FOAM represents more than just the content of the learning resources; it is considered to be an ethos, a dedication to the learning and teaching of medicine in a collaborative environment made easily accessible by online platforms.[1] These new educational platforms are changing the way learners engage with educational resources and how research is translated into practice.[3] Recent studies have demonstrated that 97.7 percent of American medical residents are spending at least one hour per week supplementing their traditional academic curricula with podcasts.[4] This rapid expansion and increasing influence of FOAM in emergency medicine suggests a need for ethical analysis. Pros and cons of FOAM from an ethical perspective are outlined in Table 1. The ensuing discussion elaborates on these key issues emergency physicians should consider when utilizing or participating in FOAM.

Patient Confidentiality

Our responsibility to protect patient privacy and health care information takes on new complexity in the FOAM and social media environment. The risks, especially when discussing clinical case vignettes or sharing radiographic or electrocardiographic content, are well described.[5] Attentive care to "de-identification" of publicly shared content requires not only removal of key patient details (eg, names, ages, and birth dates) but also more subtle identifiers such as unique conditions, events, locations, and time lines. When participating in FOAM, emergency physicians should follow the guidelines established in ACEP's forthcoming policy on use of social media.

Conflicts of Interest

The disclosure of FOAM authors' conflicts of interest should follow the same standards recognized by traditional peer-reviewed journals, namely that all professional and financial conflicts be fully disclosed to readers.[6] In FOAM, this expectation should apply not only to content authors but also commentators. A high-traffic website, social media page, or Twitter feed has significant potential value for advertising revenue. A complete ban on industry sponsorship or ad placement is not a tenable solution, as there can be substantial costs in the creation of high-quality FOAM content. Disclosing these conflicts is crucial. Transparent and reduced-bias funding sources for FOAM, such as grants, may mitigate but not reduce the risk posed by conflicts of interest.

Similar to the publication bias of journals, there may be selection bias for content that will be of interest to and shared by users. This constant pressure for innovative and engaging posts, particularly in concert with the limitations in peer review, may create content that misrepresents standard practices by emphasizing new techniques and studies. Furthermore, the lack of verification of the identity and credentials of commenters clouds the reliability of information and opens the door to covert industry infiltration, astroturfing, and other malicious intents. Social media platforms common to FOAM, as well as social media users in general, have proven to be extremely vulnerable to manipulation and dissemination of false information. There is an ethical imperative for the FOAM community to establish firm safeguards, aggressively self-regulate, and promote the skepticism that is the bedrock of scientific advancement.

Peer Review

Attempts have been made to implement formal peer review in FOAM. The blog Academic Life in Emergency Medicine (ALiEM) introduced an "expert peer review" process for providing feedback, edits, and commentary on published articles while still not delaying their release. Furthermore, there are emerging structured mechanisms to evaluate nontraditional educational sources (eg, ALiEM AIR Series and AIR Score, Medical Education Translational Resources: Impact and Quality [METRIQ], and Social Media Index).[7–10]

The open-access nature of commenting on FOAM resources does allow for a uniquely real-time appraisal. This interactive process gathers the insights of multiple practice backgrounds and experiences and is a form of ground-truthing that is not similarly available in print media. On the contrary, for FOAM in general and for comments in particular, users may be left to assess the authenticity of a statement by either the reputation of the author or the perceived accuracy of a post in a manner that is vulnerable to bias and error.

Eminence Versus Evidence

One criticism of FOAM is that it threatens a return to the time of "eminence-based" medicine rather than the evidence-based medicine that underpins modern practice. The validity of this criticism is undermined by the fact that eminent voices continue to have an amplified role in traditional educational venues. The presence of individuals with unique access to platforms and followings that allow dissemination of information is not exclusive to online communities and can be found in academic and scientific circles as well.[11,12] FOAM could be considered, in part, a reaction to the crowded space of traditional medical education and may be an attempt to democratize the process of information generation and dissemination.

Although the gold standard for medical learning remains the personal review of primary source materials, the time in which practitioners could read all of the literature relevant to their practice has long passed. Reliance on trusted sources to summarize and sort the wheat from the chaff is no longer optional. However, like any educational tool, participation in FOAM without a curricular road map can neglect and even create substantial and dangerous knowledge gaps.

There is no equivalent to PubMed for FOAM. Reliance on search engines like Goog-

le is not adequate because how search results are generated is opaque, not optimized for this purpose, and easily vulnerable to technical manipulation. A counter to this concern about locating quality information is that FOAM is about community and participation. The idea that all emergency physicians will be active participants in a worldwide community of practice is noble and exciting but improbable, and it makes the "casual" user of FOAM unlikely to reap all of its benefits and more vulnerable to its risks. This problem will only grow as more FOAM content is created.

Knowledge Translation Time

FOAM has the ability to decrease the time from knowledge discovery to knowledge integration into clinical practice, though this process continues to be less regulated than traditional methods.[1] The traditional methods of inquiry and assimilation of research findings into medical practice can take decades, with an estimated lag from time of inception to clinical practice of as much as 17 to 23 years.[13] Traditional medical journals are incorporating FOAM techniques through partnering strategies. *The Annals of Emergency Medicine* and ALiEM.com have collaborated on online journal clubs; one such encounter had 1,401 readers and 313,229 Twitter audience impressions.[14] Also, FOAM is by definition free, and eliminating the cost barrier gives it another advantage.

However, the increased speed of knowledge translation raises the question, How fast is too fast? Significant changes in clinical practice could occur before further study can verify and confirm exciting new findings.[15] Future important directions for FOAM are to establish the real-time ability to publish and discuss not only new ideas but also the structure necessary to evaluate them in standardized trials with subsequent peer review.

Distinguishing FOAM from Crowdsourcing

Crowdsourcing is the solicitation of real-time clinical input from others over an electronic platform. Distinguishing crowdsourcing from FOAM can be difficult because crowdsourcing isn't FOAM, but it may occur in the same space as FOAM activities. For example, a Twitter discussion about the best agent for blood pressure control in aortic dissection is likely FOAM, whereas tweeting, "Help!!! What should I do for my patient with an aortic dissection?" is crowdsourcing. The social media platform SERMO advertises crowdsourcing as a benefit of its network.

Crowdsourcing is a seductively appealing modern combination of informal, or "curbside," consultation and telemedicine. There is the potential benefit to provide practitioners easy access to colleagues or specialists. However, crowdsourcing lacks the robustness of telemedical consultation in terms of the amount of information shared, accountability of the consulting provider, and a mechanism to document it in the medical record. In addition, while curbside consultation (informally requesting patient management information or advice from a medical colleague) is a common practice, it has been criticized due to its greater risk of inaccurate recommendations compared to traditional consultation.[16,17] Online crowdsourcing through FOAM platforms increases these risks because the identity and credentials of those providing advice cannot be independently verified. Crowdsourcing through FOAM resources shares the appeal of FOAM itself to harness "the wisdom of crowds." However, without established processes to vet those providing input and a validated structure to balance differing views, crowdsourcing places patients at unacceptable risk.

TABLE 1: PROS AND CONS OF CHARACTERISTICS OF FOAM

CHARACTERISTIC	PRO	CON
Decrease in knowledge translation time	Decrease in the time for scientific evidence to enter clinical practice	Entry into clinical practice prior to validation has the potential to harm patients
Low barrier of entry	Allows all members of the community to contribute to the learning environment	Variable level of scholarship
Lack of traditional peer review	Crowdsourced post-publication peer review by FOAM users is continuous and may overcome the lack of traditional peer review[1]	Fewer checks and balances on the validity of information that is disseminated
No curriculum	Free to tailor resources to learner demands	Educational gaps
Worldwide access	Transcends geographical boundaries	Standards of care may differ worldwide
Self-promotion	Motivated educators can create a name for themselves in the community	The ability to self-promote online does not necessarily correspond to ability as an educator
Variable quality of content	Learners develop skills in vetting resources	Individual gestalt, regardless of the level of training, is insufficient to reliably assess online resources[18]
Forced brevity due to social media platforms	Approachable to learners	May not be sufficient to fully explain a topic
Professionalism and anonymity	Community can rapidly respond to professionalism concerns when they arise	The anonymity of online platforms allows for lapses in professional behavior
Ability to crowdsource as an informal consultation	Ability to seek assistance from others	Inability to verify credentials, lack of responsibility of those offering opinions
Multimedia	Modern learners seek multimedia resources	Use of multimedia does not necessarily correspond to the level of scholarship
Free	Accessible to all	Unpredictable costs of "free"
Conflicts of interest	Community is required to actively participate in the identification and disclosure of conflicts of interest	Disclosure of conflicts of interest is voluntary and not required for commenters, and industry infiltration may be covert and hard to identify

Conclusion

Over the last two decades, the Internet has transformed how we access information and how we learn and practice medicine. The FOAM movement has created collaborative communities capable of ultra-rapid dissemination of information and remote interaction between learners and educators. These pioneering advancements must be coupled with new responsibilities for both educators and learners. The flood of available information must be consciously processed and methodically vetted by those learning through FOAM to maintain the peer-review process and promote evidence over eminence. In addition to this responsibility, FOAM contributors also must keep patient confidentiality paramount and disclose commercial interests or involvement. FOAM will likely continue to grow and expand over time, and attention and research are needed to focus on how FOAM can best integrate with, augment, or supplant more traditional existing resources. Emergency physicians are forerunners in medical education and should continue this leadership role to ensure FOAM evolves responsibly.

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The authors are members of the ACEP ethics committee.

CLEVIPREX® (clevidipine) injectable emulsion

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CLEVIPREX® (clevidipine) is a calcium channel blocker that provides blood pressure reduction when oral therapy is not feasible or not desirable[2]

2-4 MIN onset of action[2]

~89% of acute severe hypertension patients achieved target BP[3]

~1 MIN HALF-LIFE with full BP recovery 5-15 minutes after infusion is stopped in most patients[2]

Indication

CLEVIPREX® (clevidipine) is a dihydropyridine calcium channel blocker indicated for the reduction of blood pressure (BP) when oral therapy is not feasible or not desirable.

Important Safety Information

CLEVIPREX® (clevidipine) Injectable Emulsion is contraindicated in patients with:

- Allergies to soybeans, soy products, eggs, or egg products;
- Defective lipid metabolism seen in conditions such as pathologic hyperlipemia, lipoid nephrosis, or acute pancreatitis if it is accompanied by hyperlipidemia; and
- Severe aortic stenosis.

CLEVIPREX® is intended for intravenous use. Use aseptic technique and discard any unused product within 12 hours of stopper puncture.

Hypotension and reflex tachycardia are potential consequences of rapid upward titration of CLEVIPREX®. If either occurs, decrease the dose of CLEVIPREX®. There is limited experience with short-duration therapy with beta-blockers as a treatment for CLEVIPREX®-induced tachycardia. Beta-blocker use for this purpose is not recommended.

CLEVIPREX® contains approximately 0.2 g of lipid per mL (2.0 kcal). Lipid intake restrictions may be necessary for patients with significant disorders of lipid metabolism.

Dihydropyridine calcium channel blockers can produce negative inotropic effects and exacerbate heart failure. Monitor heart failure patients carefully.

CLEVIPREX® is not a beta-blocker, does not reduce heart rate, and gives no protection against the effects of abrupt beta-blocker withdrawal. Beta-blockers should be withdrawn only after a gradual reduction in dose.

Patients who receive prolonged CLEVIPREX® infusions and are not transitioned to other antihypertensive therapies should be monitored for the possibility of rebound hypertension for at least 8 hours after the infusion is stopped.

There is no information to guide use of CLEVIPREX® in treating hypertension associated with pheochromocytoma.

Most common adverse reactions for CLEVIPREX® (>2%) are headache, nausea, and vomiting.

Please see Brief Summary on next page.

*Select patients only. CLEVIPREX is not indicated for the prevention or treatment of acute ischemic stroke.

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CLEVIPREX® (clevidipine) injectable emulsion

Brief Summary

CLEVIPREX® (clevidipine) injectable emulsion, for intravenous use

Brief Summary of Prescribing Information

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE
CLEVIPREX is a dihydropyridine calcium channel blocker indicated for the reduction of blood pressure when oral therapy is not feasible or not desirable.

CONTRAINDICATIONS
Known Allergy - CLEVIPREX is contraindicated in patients with allergies to soybeans, soy products, eggs, or egg products.

Defective Lipid Metabolism - CLEVIPREX is contraindicated in patients with defective lipid metabolism such as pathologic hyperlipemia, lipoid nephrosis, or acute pancreatitis if it is accompanied by hyperlipidemia.

Severe Aortic Stenosis - CLEVIPREX is contraindicated in patients with severe aortic stenosis because afterload reduction can be expected to reduce myocardial oxygen delivery.

WARNINGS AND PRECAUTIONS
Need for Aseptic Technique - Use aseptic technique and discard any unused product within 12 hours of stopper puncture *[see Dosage and Administration (2.3)]*.

Hypotension and Reflex Tachycardia - CLEVIPREX may produce systemic hypotension and reflex tachycardia. If either occurs, decrease the dose of CLEVIPREX. There is limited experience with short-duration therapy with beta-blockers as a treatment for CLEVIPREX-induced tachycardia. Beta-blocker use for this purpose is not recommended.

Lipid Intake - CLEVIPREX contains approximately 0.2 g of lipid per mL (2.0 kcal). Lipid intake restrictions may be necessary for patients with significant disorders of lipid metabolism. For these patients, a reduction in the quantity of concurrently administered lipids may be necessary to compensate for the amount of lipid infused as part of the CLEVIPREX formulation.

Negative Inotropy - Dihydropyridine calcium channel blockers can produce negative inotropic effects and exacerbate heart failure. Monitor heart failure patients carefully.

Beta-Blocker Withdrawal - CLEVIPREX is not a beta-blocker, does not reduce heart rate, and gives no protection against the effects of abrupt beta-blocker withdrawal. Beta-blockers should be withdrawn only after a gradual reduction in dose.

Rebound Hypertension - Patients who receive prolonged CLEVIPREX infusions and are not transitioned to other antihypertensive therapies should be monitored for the possibility of rebound hypertension for at least 8 hours after the infusion is stopped.

Pheochromocytoma - There is no information to guide use of CLEVIPREX in treating hypertension associated with pheochromocytoma.

ADVERSE REACTIONS
The following risk is discussed elsewhere in the labeling: Hypotension and Reflex Tachycardia *[see Warnings and Precautions (5.2)]*.

Clinical Trials Experience
CLEVIPREX clinical development included 19 studies, with 99 healthy subjects and 1307 hypertensive patients who received at least one dose of clevidipine (1406 total exposures). Clevidipine was evaluated in 15 studies in hypertensive patients: 1099 patients with perioperative hypertension, 126 with severe hypertension and 82 patients with essential hypertension. The desired therapeutic response was achieved at doses of 4-6 mg/hour. CLEVIPREX was infused for <24 hours in the majority of patients (n=1199); it was infused as a continuous infusion in an additional 93 patients for durations between 24 and 72 hours.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Perioperative Hypertension
The placebo-controlled experience with CLEVIPREX in the perioperative setting was both small and brief (about 30 minutes). Table 2 shows treatment-emergent adverse reactions and the category of "any common adverse event" in ESCAPE-1 and ESCAPE-2 where the rate on CLEVIPREX exceeded the rate on placebo by at least 5% (common adverse reactions).

Table 2. Common adverse reactions in placebo-controlled perioperative studies.

	ESCAPE-1		ESCAPE-2	
	CLV N=53 (%)	PBO N=51 (%)	CLV N=61 (%)	PBO N=49 (%)
Any common adverse event	27 (51%)	21 (41%)	32 (53%)	24 (49%)
Acute renal failure	5 (9%)	1 (2%)	—	—
Atrial fibrillation	—	—	13 (21%)	6 (12%)
Nausea	—	—	13 (21%)	6 (12%)

Three randomized, parallel, open-label studies called ECLIPSE, with longer exposure in cardiac surgery patients define the adverse reactions for patients with perioperative hypertension. Each ECLIPSE study compared CLEVIPREX (n=752) to an active comparator: nitroglycerin (NTG, n=278), sodium nitroprusside (SNP, n=283), or nicardipine (NIC, n=193). The pooled mean maximum dose in these studies was 10 mg/hour and the mean duration of treatment was 8 hours.

There were many adverse events associated with the operative procedure in the clinical studies of CLEVIPREX and relatively few plausibly related to the drugs used to lower blood pressure. Thus, the ability to differentiate the adverse event profile between treatments is limited. The adverse events observed within one hour of the end of the infusion were similar in patients who received CLEVIPREX and in those who received comparator agents. There was no adverse reaction that was more than 2% more common on CLEVIPREX than on the average of all comparators.

Serious Adverse Events and Discontinuation – Perioperative Hypertension Studies

The incidence of adverse events leading to study drug discontinuation in patients with perioperative hypertension receiving CLEVIPREX was 5.9% versus 3.2% for all active comparators. For patients receiving CLEVIPREX and all active comparators the incidence of serious adverse events within one hour of drug infusion discontinuation was similar.

Severe Hypertension
The adverse events for patients with severe hypertension are based on an uncontrolled study in patients with severe hypertension (VELOCITY, n=126).

The common adverse reactions for CLEVIPREX in severe hypertension included headache (6.3%), nausea (4.8%), and vomiting (3.2%). The incidence of adverse events leading to study drug discontinuation for CLEVIPREX in severe hypertension was 4.8%.

Less Common Adverse Reactions in Patients with Severe or Essential Hypertension
Adverse reactions that were reported in <1% of patients with severe or essential hypertension included:

Cardiac: myocardial infarction, cardiac arrest

Nervous system: syncope

Respiratory: dyspnea

Post-Marketing and Other Clinical Experience
Because adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate reliably their frequency or to establish a causal relationship to drug exposure. The following adverse reactions have been identified during post-approval use of CLEVIPREX: increased blood triglycerides, ileus, hypersensitivity, hypotension, nausea, decreased oxygen saturation (possible pulmonary shunting) and reflex tachycardia.

DRUG INTERACTIONS
No clinical drug interaction studies were conducted. Clevidipine and its major dihydropyridine metabolite do not have the potential for blocking or inducing any CYP enzyme.

USE IN SPECIFIC POPULATIONS
Pregnancy: Pregnancy Category C - There are no adequate and well-controlled studies of CLEVIPREX use in pregnant women. In animal studies, clevidipine caused increases in maternal and fetal mortality and length of gestation. CLEVIPREX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

There was decreased fetal survival when pregnant rats and rabbits were treated with clevidipine during organogenesis at doses 0.7 times (on a body surface area basis) the maximum recommended human dose (MRHD) in rats and 2 times the MRHD in rabbits.

In pregnant rats dosed with clevidipine during late gestation and lactation, there were dose-related increases in maternal mortality, length of gestation and prolonged parturition at doses greater than or equal to 1/6 of the MRHD based on body surface area. When offspring of these dams were mated, they had a conception rate lower than that of controls. Clevidipine has been shown to cross the placenta in rats *[see Nonclinical Toxicology (13.3)]*.

Labor and Delivery: CLEVIPREX in the labor and delivery setting has not been established as safe and effective. Other calcium channel blockers suppress uterine contractions in humans. Pregnant rats treated with clevidipine during late gestation had an increased rate of prolonged parturition.

Nursing Mothers: It is not known whether clevidipine is excreted in human milk. Because many drugs are excreted in human milk, consider possible infant exposure when CLEVIPREX is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of CLEVIPREX in children under 18 years of age have not been established.

Geriatric Use: Of the 1406 subjects (1307 with hypertension) treated with CLEVIPREX in clinical studies, 620 were ≥65 years of age and 232 were ≥75 years of age. No overall differences in safety or effectiveness were observed between these and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, for an elderly patient doses should be titrated cautiously, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

OVERDOSAGE
There has been no experience of overdosage in human clinical trials. In clinical trials, doses of CLEVIPREX up to 106 mg/hour or 1153 mg maximum total dose were administered. The expected major effects of overdose would be hypotension and reflex tachycardia.

Discontinuation of CLEVIPREX leads to a reduction in antihypertensive effects within 5 to 15 minutes *[see Clinical Pharmacology (12.2)]*. In case of suspected overdosage, CLEVIPREX should be discontinued immediately and the patient's blood pressure should be supported.

Please see Full Prescribing Information at www.cleviprex.com.

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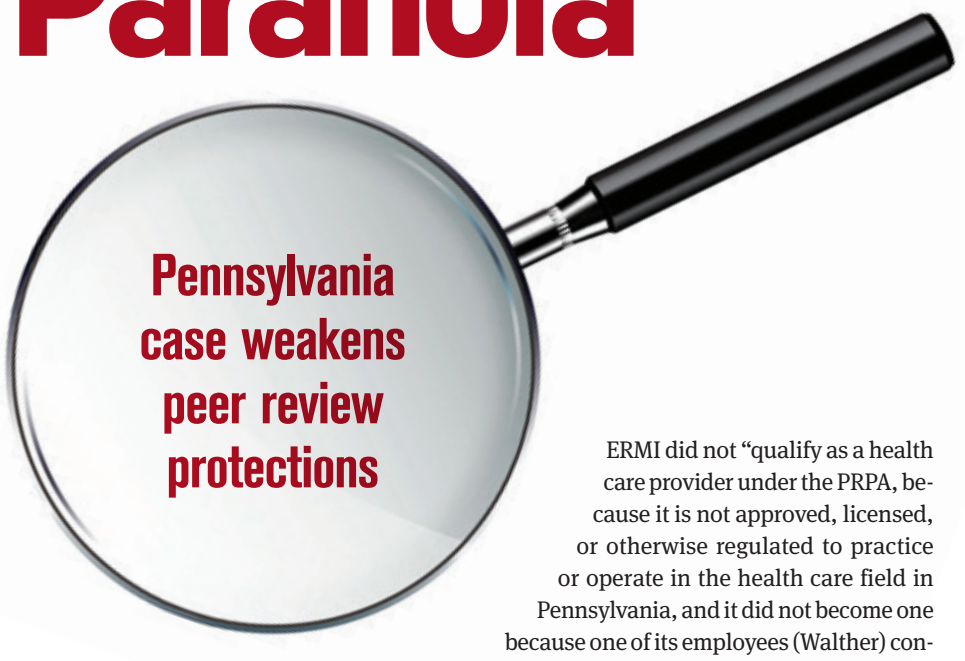
Peer-Review Paranoia



Pennsylvania case weakens peer review protections

BY KENNETH TOTZ, DO, JD, FACEP

On March 27, 2018, the the Supreme Court of Pennsylvania sent every emergency medicine contracting group scrambling to ensure their peer-review processes were comporting with the laws in their respective states. Taking a very strict interpretation of the Pennsylvania Peer Review Protection Act (PRPA), the court held that the emergency medicine contracting group, UPMC Emergency Medicine, Inc. (ERMI), did not qualify as a "professional health care provider" under the PRPA and was thus not given the evidentiary privilege afforded by the state's peer-review statute.

The court ruling stems from the medical malpractice action of *Reginelli v Boggs*. The clinical story is a seemingly familiar one in emergency medicine, whereby a patient presents to the emergency department with epigastric discomfort, returning later with a misdiagnosed myocardial infarction. The issues soon turned from the basic elements of a negligence claim to the discoverability of peer-review material. During a deposition, it became apparent that Brenda Walther, MD, the ED director, maintained a "performance file" on the physicians in the group, including the defendant, Marcellus Boggs, MD. The plaintiffs filed a motion to compel production of the performance file, which was allowed by virtue that "ERMI, as an independent contractor, is not an entity enumerated in the PRPA as being protected by peer review privilege."

The PRPA articulates that "peer review" is undertaken and protected by "professional health care providers," which are defined as those "individuals or organizations who are approved, licensed, or otherwise regulated to practice or operate in the health care field under the laws of the Commonwealth."[1] Among the 12 protected individuals or organizations listed in the act, two are "a physician and a corporation or other organization operating as a hospital."[1]

The Supreme Court of Pennsylvania affirmed the appellate court's assertion that ERMI did not "qualify as a health care provider under the PRPA, because it is not approved, licensed, or otherwise regulated to practice or operate in the health care field in Pennsylvania, and it did not become one because one of its employees (Walther) conducted an evaluation of another of its employees (Boggs)."

The court suggested that peer-review protections would have been afforded to ERMI and Dr. Boggs had Dr. Walther been a designated and documented member of the *hospital's* peer-review committee. Alternatively, the court asserted that the evidentiary privilege could have been afforded had the staffing hospital established a formal written affiliation with ERMI as an outside entity to conduct its peer-review processes for the emergency department. Although the court record alluded to an existing quasi-contractual peer-review arrangement at the trial phase of the proceedings, the agreement was not provided in a timely fashion to the court and thus became inadmissible on appellate review.

While it is a tough pill to swallow, the ruling in this case should prompt the majority of emergency medicine groups to reassess the protections their peer-review processes have in the context of the statutes in the states where they operate.

Lessons Learned

1. Review your state's peer-review statute to ensure strict compliance.
2. Confirm written affiliation between the hospital and the ED group/director to specifically perform the peer-review process.
3. Consider making the ED director or other group designee a member of the hospital peer-review process/committee.
4. Identify all peer-review personnel, materials, and processes as affirmatively falling within the peer-review statutory authority.
5. Periodically update the hospital/group agreement using language commensurate with that of the protecting peer-review statute.
6. Mark all peer-review correspondences in any form (written, oral, electronic, etc.) as protected peer-review material.

Reference

1. Pa Stat § 425.2.

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BE A MEDICAL DETECTIVE—BONE UP ON YOUR FORENSIC SKILLS

FORENSIC FACTS

DR. RIVIELLO is chair of emergency medicine at Crozer-Keystone Health System and medical director of the Philadelphia Sexual Assault Response Center.

DR. ROZZI is an emergency physician, director of the Forensic Examiner Team at WellSpan York Hospital in York, Pennsylvania, and chair of the Forensic Section of ACEP.

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Caring for ED Sexual Assault Victims

Common federal and state law requirements

by RALPH J. RIVIELLO, MD, MS, FACEP; AND HEATHER V. ROZZI, MD, FACEP

The Case

You are working a Saturday night when a 21-year-old female comes in for alcohol intoxication. Her vital signs are stable, and she appears visibly intoxicated. She appears withdrawn and tearful, and shortly after evaluation, she confides in you that she was raped at a college party. She doesn't want the police called but does want a rape kit collected. She continues to insist on no police involvement. You are unsure about collecting a kit without law enforcement involvement and do not have a sexual assault nurse examiner (SANE) team at your hospital. What do you do?

It's Not Unusual

Sexual assault is a common complaint in the emergency department. A 2010 study showed that one in five women and one in 71 men will experience rape, which the authors defined as "forced attempted or completed penetration."[1] The rates of sexual violence other than rape, including being forced to penetrate another person, sexual coercion, unwanted sexual contact, and non-contact unwanted sexual experiences, are experienced by one in two women and one in five men sometime during their life.[1] And these national statistics do not adequately reflect the experience of populations in which rape and sexual violence occur in much higher numbers.

How patients are cared for in the emergency department can have profound effects on their physical, psychological, and emotional healing. Well-functioning, victim-centered programs utilizing SANE teams have been perceived as helpful, caring, compassionate, and supportive by sexual assault victims. Survivors are left feeling supported, believed, heard, respected, safe, reassured, in control, informed, and well cared for post-assault.[2–4] In contrast, a negative ED experience following sexual assault produces the opposite effects.

What Does the Law Require?

Emergency physicians are often held to federal and/or state laws when caring for victims of crime, including sexual assault survivors. Several of these laws come into play in the above case as well as in the overall care of intoxicated sexual assault patients.

First, many state statutes mandate law enforcement notification when patients who are victims of certain crimes present to the emergency department. These include gunshot wounds, stab wounds, battery, assaults with weapons, child abuse, elder abuse, domestic abuse, and sexual assault. For these crimes, ED personnel are classified as mandated reporters.

But just because a state law mandates reporting does not mean the patient has to speak to police. It is well within the rights of the patient to refuse to cooperate with law enforcement. Police understand this discrepancy between the law and the victim's autonomy. Police officers may also be able to better explain to the patient all of their options regarding sexual assault reporting and investigation as well as the benefits and potential downsides of reporting. Sometimes officers develop a rapport with patients and may convince them to report the crime.

States may have victims' rights laws, which provide protections and rights to crime victims. Some states require the patient be given the option of having a rape crisis advocate present during their examination. The hospital must inform the patient of this right and notify the advocate for the patient. In most jurisdictions, communication between the victim and

CONTINUED *on page 31*

KEY POINTS

- Sexual assault is common, and emergency departments are where many survivors seek care.
- The ED experience can have a positive or negative impact on survivors and their healing.
- State and local laws can significantly impact sexual assault care provided in the emergency department.
- The Violence Against Women Act allows for examination to occur without law enforcement participation.
- Emergency departments should have clear and concise policies for managing unconscious, incapacitated, or intoxicated victims.

DR. AUGUSTINE is chair of the National Clinical Governance Board of US Acute Care Solutions in Canton, Ohio; clinical professor of emergency medicine at Wright State University in Dayton, Ohio; vice president of the Emergency Department Benchmarking Alliance; and a member of the ACEP Board of Directors.

ED Inefficiency Drives Poor Quality

The data shows how we can reduce the number of patients who leave before completing treatment

by JAMES J. AUGUSTINE, MD, FACEP

Emergency departments face significant challenges in patient management and concomitant increases in regulatory and reporting requirements. Some regulatory requirements are matched to transparency mandates for items that will be reported to the public, such as the Hospital Compare measures from the Centers for Medicare and Medicaid Services. And notably, the issues of timely care, flow through the emergency department, and safety incidents in the ED waiting room have activated regulators, The Joint Commission, and the general media.

ED leaders have tackled the critical imperative to reduce the number of persons who enter the emergency department but leave prematurely. The Emergency Department Benchmarking Alliance (EDBA) has worked with other organizations to develop definitions that provide consistency in reporting. With the input of ED leaders who recognize the temptation to cheat on this reporting element, it was necessary to develop an inclusive term that would incorporate all patients who leave before they are supposed to and would *not* provide gaps for patient encounters to be missed in the ED reporting systems.

The participants in the third Performance Measures and Benchmarking Summit have published the results of the sessions in which ED definitions were developed, with incomplete ED patient encounters termed "left before treatment complete" (LBTC).[1] This single definition provides the most complete accounting for all patients who leave the emergency department before they are supposed to, and it includes patients who leave before or after the EMTALA-mandated medical screening examination, those who leave against medical advice (AMA), and those who elope (ie, simply walk out without speaking to anyone).

The EDBA uses this single statistic to compile the annual number of patients who are recognized by the emergency department but leave prior to completion of treatment. This provides the most complete accounting for all incomplete encounters, and it delivers a great comparison statistic.

The Stats

A number of studies have related ED walkaway rates to flow rates, and across a 14-year time frame, the EDBA data have found walkaway rates relate to volume, ED type, time to first contact with a licensed provider, and overall ED flow.[2,3] The LBTC rate has trended lower across EDBA hospitals over the prior 14 years (see Figure 1).

For the past eight years, the EDBA study has evaluated various time intervals and their potential contribution to the LBTC rate. Table 1 shows the eight-year data on LBTC and median door-to-provider and door-to-decision times for admitted patients. Despite a consistent drop in median door-to-provider times, the LBTC rate has gone up, possibly because during those eight years the door-to-decision time has crept higher. That time is generally under the control of the emergency physician, and it offers an opportunity to focus on efficiencies that will move critical information to emergency physicians so they can make a quality decision.

In 2017, the LBTC rate was 2.7 percent across all emergency departments, but it varied significantly across the various cohorts that represent different types of emergency departments and different ED volumes. The LBTC rate by cohort appears in Figure 2.

Table 2 shows the EDBA time intervals and LBTC rate. That data suggests a correlation between processing all patients, the door-to-decision time for admitted patients, and overall walkaway rates. And it clearly reflects the stresses on ED operations when volume and patient acuity increase.

The overall complexity of processing patients who ultimately are admitted is reflected in the amount of time it takes across all cohorts to arrive at the decision to admit. Even in the smallest emergency departments, the median time to that decision was 164 minutes. The other ED cohorts reported a time range of roughly 180–228 minutes, except for the group of emergency departments in the 100,000–120,000 volume range, where the time to decision averages 273 minutes. Long time intervals to decision to admit or discharge are associated with higher LBTC rates.

Conclusions

We can see emergency physicians have an opportunity to reduce walkaway rates by improving decision timing. Many emergency departments have reduced door-to-provider time, but we also need a timely effort to perform diagnostic testing and get the results to the responsible emergency physician, initiate any necessary treatment and evaluate the results, conduct necessary conversations with primary care or other consulting physicians, and complete a review of pertinent medical

FIGURE 1: PERCENTAGE OF PATIENTS WHO LBTC, 2004–2017

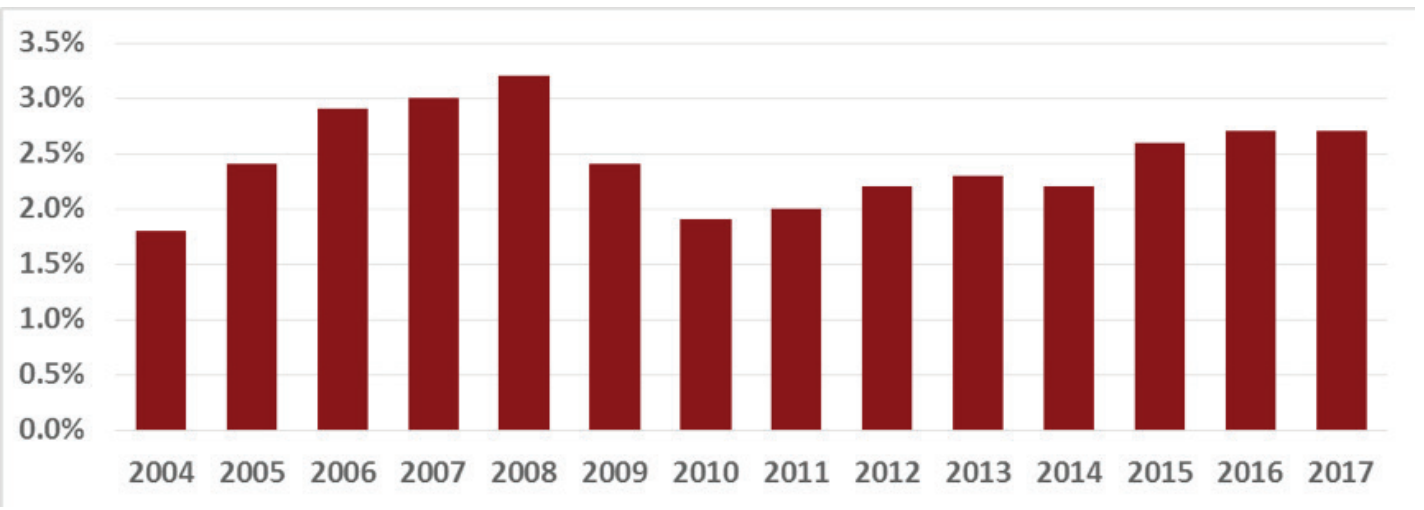

TABLE 1: DOOR-TO-PROVIDER, LENGTH-OF-STAY, AND LBTC TRENDS, 2010–2017

YEAR	MEDIAN DOOR-TO-PROVIDER TIME (MINUTES)	MEDIAN LENGTH OF STAY, DOOR-TO-DECISION FOR ADMITTED PATIENTS (MINUTES)	LBTC
2010	33	151	1.9%
2011	30	185	2.0%
2012	32	168	2.2%
2013	30	176	2.3%
2014	28	186	2.2%
2015	28	189	2.6%
2016	27	185	2.7%
2017	25	186	2.7%

records. All of those items combined will give the emergency physician an opportunity to make a quality disposition decision and initiate transition of care.

Decision to admit by an emergency physician begins a cascade of events that should end in a timely movement of the patient to the inpatient unit. A boarding time discussion took place in a 2016 *ACEP Now* article, but unfortunately the EDBA boarding time numbers in 2016 and 2017 remained consistent at about 117 minutes.[4]

Despite ED volume and acuity increases that challenge ED providers, improved operations have been evident in many emergency departments. However, the LBTC rates relate to ED efficiency and processing, and improving those areas requires coordinated utilization of staff, equipment, processes, and documentation.

Bottom line: Opportunities to improve patient flow *do* exist, and improved patient flow will reduce the rate of incomplete patient encounters.

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FIGURE 2: LBTC PERCENTAGES IN VARIOUS ED COHORTS (AVERAGE: 2.7%)

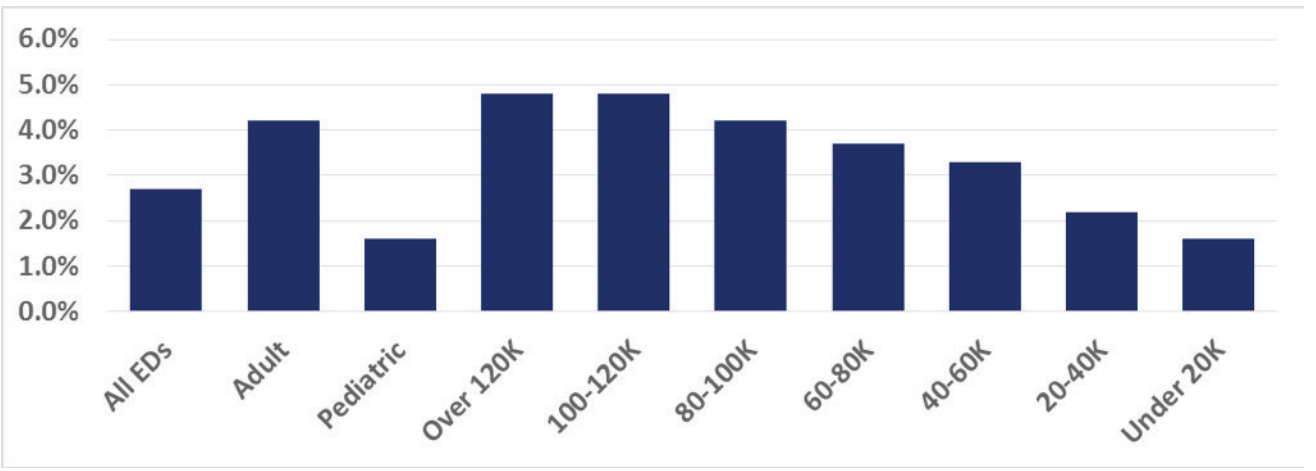

TABLE 2: 2017 EMERGENCY DEPARTMENT BENCHMARKING ALLIANCE DATA SURVEY RESULTS

ED TYPE	MEDIAN LENGTH OF STAY, ALL ED PATIENTS (MINUTES)	MEDIAN DOOR-TO-DECISION TIME, ADMITTED PATIENTS (MINUTES)	LBTC
All EDs (N=1,717)	181	186	2.7%
Under 20K volume	134	164	1.6%
20–40K	164	173	2.2%
40–60K	200	209	3.1%
60–80K	222	213	3.8%
80–100K	242	229	4.3%
100–120K	245	273	4.8%
Over 120K volume	228	228	4.9%
Pediatric EDs	149	187	1.6%
Adult EDs	247	225	4.2%

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advocate are privileged. Rape crisis center advocates understand the many ways sexual assault can impact a person and their family and are there to provide support and information so that the survivor may make informed, critical decisions. Advocates may also intervene or act on behalf of the survivor and assist with navigating the processes within the medical, law enforcement, and court systems.

Some states may have emergency contraception (EC) laws that require hospitals to provide emergency contraception to sexual assault survivors.[5] If EC is not provided on site, such laws require the hospital have alternative plans for patients to obtain the medication. Some states require hospitals to register with the state and provide patient notification of the lack of provision of these resources.

Finally, and most important, federal laws play a role in sexual care. The Violence Against Women Act (VAWA) was passed in 1994 and has been reauthorized in 2000, 2005, and 2013.[6,7] VAWA provides communities with tools and funding to improve response to victims of sexual assault, domestic violence, dating violence, stalking, and trafficking. The act includes access to examinations free of charge, regardless of victim cooperation with law enforcement. Every state receives VAWA funding to provide services to sexual assault survivors.

One of the enhancements to VAWA in 2005 required states, as a condition of funding, to allow victims to receive a medical forensic examination without having to report the crime to law enforcement.[6–8] These kits have become known as Jane/John Doe kits or anonymous kits. This process allows victims to access medical care and allows time-sensitive evidence to be collected without forcing victims to immediately decide whether to report the rape to law enforcement. Victims can report the crime at any time to law enforcement within a prescribed time frame (which is state-dependent), and the collected evidence can then be analyzed. Giving victims time to decide about reporting is important for returning power to victims and giving them control over their participation with the criminal justice system. Failure to follow the VAWA statutes can cause a state to lose its VAWA funding.

One key tenet of sexual assault care is that patients must be able to provide consent for the medical forensic examination; patients have the right to refuse any or all parts of the examination.[9,10] Also, they have the right to decide what happens with the evidence collected.

Patients who are intoxicated may be not be capable of providing informed consent or actively participating in the exam process due to their level of intoxication. In these cases, patients should be observed and allowed time for detoxification. After clinical sobriety, options regarding reporting and the medical forensic examination can be re-reviewed with patients. Some patients who are unconsciousness, head-injured, or have other serious traumatic or medical conditions may remain unable to consent for a much longer period. During this prolonged period, evidence may be lost or degraded. Therefore, emergency departments should have protocols for handling consent and examination in these unconscious/non-

CONTINUED *on page 33*

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5-Step Approach to the Agitated Patient

Stick to your plan to "keep it chill"

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

We're all familiar with the spike in cortisol levels we feel when faced with agitated patients in the emergency department. That's not only because of our hard-wired fight-or-flight response but also because we know that these patients are high-risk to themselves, us, and our ED staff. Agitation or agitated delirium is not a diagnosis but rather a cardinal presentation. Pathology, such as psychiatric, medical, traumatic, and toxicological diagnoses, is lurking beneath; it is imperative that we safely and rapidly calm these patients so we can assess and manage their underlying diagnoses. Here is a five-step approach to managing agitated patients.

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Step 1: Categorizing Agitation as Mild, Moderate, or Severe

It is helpful to categorize the level of agitation to better target sedation. The mildly agitated patient is able to converse and is cooperative without being disruptive, while the moderately agitated patient is disruptive to your emergency department without imminent danger to themselves or your ED staff. However, the severely agitated patient is imminently dangerous to all. This last category includes patients with excited delirium syndrome, a true emergency with a very high mortality rate. Excited delirium syndrome has several distinctive features that include unusual superhuman strength, imperviousness to pain, severe metabolic acidosis, inability to maintain attention, and hyperthermia.[1]

Step 2a: Nonpharmacologic De-escalation for Mildly or Moderately Agitated Patients

Verbal de-escalation is often effective in the mildly to moderately agitated patient, but it requires a calm and deliberate approach.[2] Some key elements of effective de-escalation include environmental awareness and self-awareness, such as delegating one person to speak to the agitated patient, ensuring a quiet room, modulating your own emotional and physiologic responses to remain calm, avoiding clenched fists, and having your hands visible.

The SAVE mnemonic outlines scripted responses that may be helpful when faced with a violent patient:[3]

- **Support:** "Let's work together..."
- **Acknowledge:** "I see this has been hard for you."
- **Validate:** "I'd probably be reacting the same way if I was in your shoes."
- **Emotion naming:** "You seem upset."

Step 2b: "Code White" for Moderately and Severely Agitated Patients

Consideration should be given to calling a "code white" for the patient who is an immediate physical threat to you or your staff. A common pitfall is to call a code white as a threat to an uncooperative patient, which can inadvertently increase agitation. Consider calling a concealed code white, directly to security, rather than using an overhead page for the moderately agitated patient who is not posing an imminent danger.

Step 3: Safe and Effective Physical Restraints

There is ongoing debate as to whether physical restraints should be used at all in the management of the agitated patient in the emergency department. If you are going to use physical restraints, the goal should be to use them only as a last resort as a bridge to chemical restraint, which should take no longer than five to 15 minutes with appropriate dosing.[4] Prolonged use of physical restraints may result in active resistance of restraints, which may lead to electrolyte abnormalities or dysrhythmias and put the patient at further risk for rhabdomyolysis.

One option is to avoid the use of physical restraints and instead hold the patient down by security for the few minutes it takes for the calming medications to take effect. The other option is to place the physical restraints on the patient, immediately administer intramuscular (IM) calming medications, and release the restraints as soon as the patient is calm. Physical restraints should always be followed by immediate sedation.

When used properly, physical restraints can be quite safe.[5] However, improper use can be lethal. In one study, 26 deaths were presumed to be the direct result of improper physical restraints.[6] Avoid covering the agitated patient's mouth and/or nose with a gloved hand. This can lead to asphyxia, metabolic acidosis, and death. Use an oxygen mask to prevent the patient from spitting on staff. This may also serve to improve oxygenation. With the patient in the supine position with about 30 degrees head elevation, use four-point restraints tied to the bed frame (rather than the rails), with one arm above the head and the other below the waist.

Step 4: Chemical Restraint or Sedation

The goal of calming medications is to enable rapid stabilization of the acutely agitated patient and to enable the expeditious search for potential life-threatening diagnoses. The choice of route depends on how agitated your patient is. For cooperative mildly agitated patients, offer oral or sublingual medications first. For uncooperative moderately and severely agitated patients, the safest option is to start with IM medications.

Calming medication options include ketamine, benzodiazepines, and antipsychotics.

Whenever possible, tailor the therapy to the underlying diagnosis (eg, psychotic psychiatric disorder, alcohol withdrawal, drug intoxication, etc.). While the evidence for one regimen over another is lacking, current evidence-based recommendations are summarized in Table 1.

IM midazolam is the best benzodiazepine option in moderately to severely agitated patients as it is quickly and reliably absorbed.

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TABLE 1: CALMING MEDICATION RECOMMENDATIONS FOR AGITATED PATIENTS[7–13,16]

LEVEL OF AGITATION	FIRST-CHOICE DRUG, DOSE, ROUTE	ALTERNATIVE OR ADJUNCT DRUG
Mild	Lorazepam 1–2 mg sublingual	Oral antipsychotic that has previously been effective for that patient
Moderate	Midazolam 2–5 mg IM	Haloperidol 5–10 mg IM
Severe	Ketamine 5 mg/kg IM	Haloperidol 10 mg IM and midazolam 10 mg IM

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consentable patients.

Many advocate for collecting the evidence and then waiting for patients or their legal surrogate to decide what is done with the evidence. Emergency departments and SANE programs should have a policy describing how to handle intoxicated, unconscious, or incapacitated victims of sexual assault.[9]

Case Resolution

The patient remains hemodynamically stable and is allowed to sober up in the emergency department. At that time, the patient still wants to undergo medical forensic examination without reporting the incident to the police. The patient is transferred to a SANE-designated facility and undergoes examination and evidence collection.

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In alcohol-intoxicated patients, beware of respiratory depression with benzodiazepines and place them on a cardiac monitor, ideally with end-tidal CO_2 monitoring for early detection of respiratory depression.

Haloperidol should be considered an adjunct to benzodiazepines for moderate and severe agitation and may be appropriate as monotherapy in moderately agitated intoxicated patients who cannot be placed on a monitor when resources are limited.[7–9] Be aware that haloperidol has a longer half-life than midazolam, which can result in the patient staying in your emergency department for much longer than would be necessary otherwise. Although haloperidol prolongs the QTc, this effect is very unlikely to be clinically consequential at the doses typically used for emergency agitation. Nonetheless, caution is advised in patients who are already taking multiple QTc-prolonging agents. Consider obtaining a baseline ECG first in these higher-risk patients.

Ketamine is an N-methyl-D-aspartate receptor antagonist, providing rapid sedation and analgesia. Of the available options, its time to sedation is the fastest, usually less than five minutes with appropriate dosing. Current evidence for the effectiveness and safety of ketamine in calming the severely agitated patient is promising but not definitive.[11–13]

Step 5: Treating Immediate Life Threats and Pursuing Underlying Diagnosis as Soon as Calming Medications Take Effect

For the mildly to moderately agitated patient, corroborating the history with a head-to-toe physical exam with the patient completely disrobed is essential. Consider a broad differential diagnosis, including space-occupying central nervous system lesions as well as toxicological, psychiatric, traumatic, and metabolic causes.

For the severely agitated patient, it is important to be organized in your approach, which can be divided into the first few minutes, the next few minutes, and the next hour.

In the first few minutes, place the patient in a resuscitation room and apply cardiorespiratory monitoring, capnography, and oximetry. Initiate one to two large-bore peripheral IVs and assess for and start to treat the four Hs: hypoxia, hyperthermia, hypovolemia, and hypoglycemia. If a definitive airway is required, consider delayed sequence rather than rapid

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sequence intubation, including hyperventilation and sodium bicarbonate in the peri-intubation period as the patient may be severely acidotic.[14,15] In the next few minutes, obtain electrolytes and blood gas and treat for hyperkalemia and acidemia. Consider a head CT scan. In the next hour, consider primary diagnoses such as sepsis, neuroleptic malignant syndrome, thyrotoxicosis, and meningitis/encephalitis. In addition, it is important to assess for consequences of agitation (eg, rhabdomyolysis and traumatic injuries).

Having a simple approach to the agitated patient in the emergency department will not only buffer your cortisol levels but also give you the tools you need to safely and efficiently uncover and manage a life-threatening diagnosis.

Special thanks to Dr. Margaret Thompson and Dr. Reuben Strayer, the guest experts on the podcast from which this column was inspired.

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CODING WIZARD

NAVIGATE THE CPT MAZE, OPTIMIZING YOUR REIMBURSEMENT

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

DOCUMENTING WOUND DEBRIDEMENT

by **HAMILTON LEMPERT, MD, FACEP, CEDC**

Question: How do I code for a wound debridement?

Answer: Current Procedural Terminology (CPT) provides several different coding options for reporting wound debridement service, depending on the type of debridement performed. The most common codes used in the emergency department are 97597 (0.68 relative value units [RVU], $24 for Medicare) for debridement involving the epidermis and/or dermis and 11042 (1.78 RVU, $64 for Medicare) for debridement of subcutaneous tissue. The deepest layer of tissue debrided determines which code to use. Each of these codes is for 20 cm^2 or less, and there are additional codes to use when more than 20 cm^2 are debrided, 97598 and 11045, respectively. Ideal documentation for debridement should include the depth of tissue (layers) debrided as well as the total surface area of the wound. There are also debridement codes for muscle or fascia (11043) and bone (11044) when performed by the emergency department provider.

Brought to you by the ACEP Coding and Nomenclature Committee.

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

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Statement of Ownership, Management, and Circulation (Requester Publications Only)

1. Publication Title	2. Publication Number	3. Filing Date
ACEP Now	2 4 5 – 6 4	10/1/2018
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price (if any)
Monthly	12	$278

7. Complete Mailing Address of Known Office of Publication *(Not printer) (Street, city, county, state, and ZIP+4®)*
Wiley Subscription Services, Inc., 111 River Street, Hoboken, NJ 07030

Contact Person: E. Schmidichen
Telephone *(Include area code)*: 201-748-6346

8. Complete Mailing Address of Headquarters or General Business Office of Publisher *(Not printer)*
Wiley Subscription Services, Inc., 111 River Street, Hoboken, NJ 07030

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor *(Do not leave blank)*

Publisher *(Name and complete mailing address)*
Wiley Subscription Services, Inc., 111 River Street, Hoboken, NJ 07030

Editor *(Name and complete mailing address)*
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ACEP Now	September 2018

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