N E W S L E T T E R

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E Komo Mai!

Welcome to the SOCCA 28th Annual Meeting and Critical Care Update in Honolulu!

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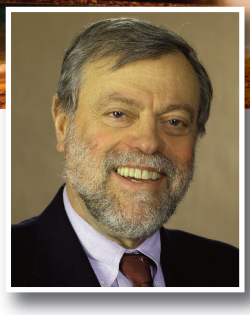

Aryeh Shander, MD, FCCM, FCCP
President of SOCCA; Chief, Department of Anesthesiology, Critical Care Medicine, Pain Management and Hyperbaric Medicine at Englewood Hospital and Medical Center, Englewood, New Jersey; Clinical Professor of Anesthesiology, Medicine and Surgery, Icahn School of Medicine at Mount Sinai, New York, New York

Contents

Aloha!

Welcome to the Society of Critical Care Anesthesiologists (SOCCA) 28th Annual Meeting and Critical Care Update in Honolulu, Hawaii! We are happy you have joined us for two days of stimulating critical care education, led by the leaders in critical care anesthesia. This energizing education program will address your specialized needs as an intensivist as well as your broader needs as a practicing anesthesiologist. We hope you will find this time together, for learning and networking opportunities, rewarding and will take away the valuable knowledge you need to advance your research and practice!

Gain quality one-on-one time with the thought leaders in critical care in an intimate, relaxed atmosphere. Visit with exhibitors and test the latest innovations. Map out your education plan and make the most of your time at the Annual Meeting! Download the Final Program now at http://www.socca.org/2015-final-program.pdf to discover the sessions and networking opportunities that will be most helpful to you. Make sure to attend the Reception with Exhibitors, from 5:45 pm to 7:00 pm, and experience the spirit of aloha while building new connections.

The SOCCA 28th Annual Meeting and Critical Care Update will kick-off with a session focused on *Acute Infectious Disease in the ICU*. Topics include care of the Ebola-infected patient in the critical care unit,

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Welcome to the SOCCA 28th Annual Meeting and Critical Care Update in Honolulu!

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infectious risks to healthcare workers in the ICU, and disaster management in the ICU. The second session, *New Evidence, New Investigations and New Directions,* will present the important publications critical care anesthesiologists should know to advance their practice and research plus highlights the Young Investigator Award recipient.

SOCCA will also honor two award winners during the Annual Meeting for their achievements and advancements in critical care anesthesiology. Dr. Christina J. Hayhurst will be awarded the Young Investigator Award for her abstract presentation, *Chronic Pain Interference of Daily Life Following Critical Illiness.* Dr. Philip G. Boysen will also be recognized for his significant achievements in critical care with the Lifetime Achievement Award. He accepted the award and will deliver an inspiring presentation, entitled, *Eyewitness to Leadership: Examining Our Past, Forecasting Our Future.*

SOCCA strives to expand the learning opportunities and resources available to its members and critical care anesthesiologists and this meeting is a representation of that focus. SOCCA continues to bring cutting-edge updates in clinical and basic science research for critical care from the leaders in critical care anesthesia to a wide audience, including the IARS Annual Meeting. The SOCCA 28th Annual Meeting and Critical Care Update, on Friday, March 20, 2015 in Honolulu, Hawaii, is the second meeting aligned with the International Anesthesia Research Society (IARS). At the IARS 2015 Annual Meeting and International Science Symposium, for the first time, SOCCA is supporting a Focus on Critical Care Day with two Panels, two Review Course Lectures, a workshop and a Problem-Based Learning Discussion.

With double the learning opportunities, attendees are able to take advantage of two full days of invigorating critical care education sessions and networking opportunities at no additional charge. This expanded program champions SOCCA's mission to advance the education of anesthesiologists in the care of critically ill patients and to foster the knowledge and practice of critical care medicine by anesthesiologists.

SOCCA continues to value and provide resources to young and promising anesthesiologists in the field, fostering the next generation of leaders in critical care. A special resident program offers these up-and-coming leaders valuable knowledge and career development tips as part of the SOCCA 28th Annual Meeting and Critical Care Update. Additionally, the SOCCA mentorship program matches resident attendees with mentors to offer another perspective on critical care and the guidance needed to successfully navigate the next path in their career development.

In 2016, SOCCA will further expand its educational offerings by aligning its Annual Meeting for the first time with both the Association of University Anesthesiologists (AUA) and the IARS in San Francisco. The alignment of the SOCCA, AUA and IARS Annual Meetings is just the beginning. SOCCA will continue to look for new ways to provide critical care anesthesiologists with the knowledge they need to succeed in their career and dedicate its efforts to advance the care of critically ill patients and to foster the knowledge and practice of critical care medicine by anesthesiologists. For now, take in the beautiful, majestic scenery in Hawaii, absorb new knowledge, and network with your colleagues and peers! We are confident you will make the most of all that Hawaii and the SOCCA 28th Annual Meeting and Critical Care Update have to offer!

Mahalo!

Editorial Notes

A Note from the Editor to SOCCA Members:

If you would like to contribute a review for a Fellowship Program at your institution in a future issue of the SOCCA Interchange, please contact: **jbrandmd@gmail.com**

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E Komo Mai!

Welcome to the SOCCA 28th Annual Meeting and Critical Care Update in Honolulu, Hawaii!

The Society of Critical Care Anesthesiologists (SOCCA) will hold the SOCCA 28th Annual Meeting and Critical Care Update in conjunction with the International Anesthesia Research Society (IARS) 2015 Annual Meeting and International Science Symposium. Take advantage of a solid two-day education program, beginning with the SOCCA 28th Annual Meeting on March 20 and continuing with a full day focused on critical care at the IARS 2015 Annual Meeting on March 21.

During this stimulating program, discover the latest updates in the practice of critical care medicine, original investigations in the clinic and laboratory, presented by your colleagues during the Moderated Poster Sessions, and multiple opportunities for networking including an upbeat reception, in the *spirit of aloha*, to conclude the meeting.

Below are some of the highlights of the Annual Meeting.

Session I
The SOCCA 28th Annual Meeting will kick off with a session focused on *Acute Infectious Diseases in the ICU*. Topics include: Care of the Ebola-infected patient in the critical care unit, infectious risks to healthcare workers in the ICU, and disaster management in the ICU.

Session II
The second session, *New Evidence, New Investigators and New Directions*, presents the important publications critical care anesthesiologists should know to advance their practice and research plus highlights the Young Investigator Award recipient.

Session III
The third session of the day, *Atrial Fibrillation: An Update You Won't Want to Miss* discusses monitoring of patients at risk of perioperative atrial fibrillation, the best approach for diagnosis, prevention and management of this condition, as well as the appropriate use of cardiology and electrophysiology consults.

Session IV
The fourth session identifies and examines controversial management issues in high risk perioperative care.

Focus on Critical Care Day – March 21

The Saturday IARS education program offers a special focus on critical care including two Panels, two Review Course Lectures, a Workshop and a Problem-Based Learning Discussion session:

- SOCCA Panel: *Critical Care for the Nonintensivist – What You Need to Know*
- SOCCA Panel: *Coordinating Perioperative Care Across the Continuum: Defining Roles and Responsibilities for Managing the Critically Ill Patient*
- SOCCA RCL: *Anesthesia Advanced Circulatory Life Support*
- SOCCA RCL: *Ebola: Care of the Patient and the Anesthesiologist*
- SOCCA Workshop: *Critical Care Ultrasound Workshop*
- SOCCA PBLD: *Congenital Heart Disease for Noncardiac Surgery?*

We are confident that you will find these two days of critical care sessions to be rewarding! Enjoy the sun-filled days, turquoise seas, gorgeous scenery, and all that Honolulu has to offer!

Sincerely,

SOCCA Annual Meeting Program Committee

Patricia Murphy, M.D.
Daryl J. Kor, M.D., MSc
Andrew C. Steel, B.Sc., MBBS, MRCP, FRCA, FRCPC, EDIC

Program Schedule

Friday, March 20, 2015

7:00 a.m. – 5:00 p.m. **Registration**

7:00 – 7:30 a.m. **Coffee with Exhibitors**

7:30 – 8:00 a.m. **Continental Breakfast**

8:00 – 8:05 a.m. **Welcome and Introduction**
Patricia Murphy, M.D.
Andrew C. Steel, BSc., MBBS

SESSION I – Acute Infectious Diseases in the ICU

Patricia Murphy, M.D. – Moderator

8:05 – 10:00 a.m. **Care of the Ebola Infected Patient in the Critical Care Unit, What You Need to Know**
James N. Sullivan, M.D.

Infectious Risks to Healthcare Personnel in the ICU
Patricia Murphy, M.D.

Disaster Management in the ICU: Are We Ready for the Next Pandemic?
Steven J. Lisco, M.D., FCCM, FCCP

10:00 - 10:30 a.m. **Break with Exhibitors**

SESSION II – New Evidence, New Investigators and New Directions

10:30 – 11:30 a.m. **Important Publications You Might Have Missed**
Joseph A. Hyder, M.D., Ph.D. – Moderator
Panelists: Erin Hennessey, M.D.
Christopher G. Hughes, M.D.

11:30 – 11:45 a.m. **Young Investigator Award and Abstract Presentation**
"Chronic Pain Interference of Daily Life Following Critical Illness"
Christina J. Hayhurst, M.D.

11:45 a.m. – Noon **ASA Address**
Daniel J. Cole, M.D.
ASA President-Elect

Noon – 1:15 p.m. **Lunch**

SESSION III – Atrial Fibrillation: An Update You Won't Want to Miss!!

Gyorgy Frendl, M.D., Ph.D., FCCM – Moderator

1:20 – 2:25 p.m. **Perioperative Atrial Fibrillation: Its Incidence, Impact and Effective Prevention Strategies**
Alissa C. Sodickson, M.D.

Recommended Management of Perioperative Atrial Fibrillation
Gyorgy Frendl, M.D., Ph.D., FCCM

Genetics of Perioperative Atrial Fibrillation – The Hope for Personalized AF Care
Martin I. Sigurdsson, M.D., Ph.D.

Discussion

2:30 – 3:00 p.m. **Lifetime Achievement Award Presentation**
"Eyewitness to Leadership: Examining Our Past, Forecasting Our Future"
Philip G. Boysen, M.D.

3:00 – 3:30 p.m. **Moderated Poster Session**

3:30 – 3:45 p.m. **Break with Exhibitors**

SESSION IV – Interactive Case Management

3:45 – 4:55 p.m. **Interactive Case Management**
Avery Tung, M.D., FCCM – Moderator
Panelists: Miguel A. Cobas, M.D., FCCM
Brenda G. Fahy, M.D., MCCM
Breandon Sullivan, M.D.

4:55 – 5:00 p.m. **Closing Remarks**

5:00 – 5:45 p.m. **SOCCA Annual Business Meeting**

5:00 – 6:00 p.m. **Resident/Fellow Program**

5:45 – 7:00 p.m. **Reception with Exhibitors**

A Review of Prothrombin Complex Concentrates

Sheida Tabaie, MD
Adult Critical Care Fellow
Department of Anesthesiology
New York Presbyterian Hospital
Weill Cornell Medical College
New York, New York

James Osorio, MD
Assistant Professor of Anesthesiology
Program Director Anesthesiology
Critical Care Medicine
Department of Anesthesiology
New York Presbyterian Hospital
Weill Cornell Medical College
New York, New York

Introduction:

Prothrombin complex concentrates (PCCs) are becoming an integral part of transfusion medicine's armamentarium in the United States. Originally developed as a treatment for patients with hemophilia B, PCCs are now predominantly used for the urgent reversal of vitamin K antagonist (VKA) therapy.[1] This review will provide an overview of PCC products, the indications for PCC use, the complications associated with PCC use, recent data comparing PCC to fresh frozen plasma for urgent VKA reversal, and the novel ways in which PCC is now being employed.

PCC Overview:

PCCs are derived from large pools of plasma after removal of anti-thrombin and factor XI using ion-exchange chromatography.[2] Depending on the processing technique employed, the result is either a three-factor or a four-factor concentrate with an overall clotting factor concentration that is approximately 25 times higher than that in normal plasma.[2] To prevent activation, most PCCs contain heparin and some contain anti-thrombin III; they may also contain the natural coagulation inhibitors protein C and protein S. To minimize infection transmission, every PCC undergoes at least one round of viral reduction or elimination prior to completion.[2] PCCs consist of a combination of vitamin K-dependent coagulation factors, with factor IX standardized across most preparations. For the majority of PCCs, these factors are inactivated and require activation via the coagulation cascade.[3] 3-Factor PCCs predominantly contain factors II, IX and X. 4-Factor PCCs contain factors II, VII, IX, and X.

As highlighted in the table below, it is important to recognize that each PCC brand has a unique composition, consisting of different amounts of both coagulation factors and anticoagulants. The PCCs currently available in the United States include two 3-Factor PCCs (Profilnine® and Bebulin® VH), one 4-Factor PCC (Kcentra®), and the activated 4-Factor PCC (FEIBA®). Studies directly comparing 3-Factor PCCs to 4-Factor PCCs, or inactivated 4-Factor PCC to activated 4-Factor PCC are lacking.[3] However, 4-Factor PCCs are thought to be more effective than 3-Factor PCCs because they replace all of the deficient vitamin K-dependent clotting factors; thus, 4-Factor PCC should be used when available. If 3-Factor PCC must be used, it is advisable to administer it with a small amount of FFP in order to ensure a source of factor VII.[4, 5]

Table 2. Major Prothrombin Complex Concentrates: Availability and Composition[35-44]

		Factor Levels (IU/mL)[a]				Protein Levels (IU/mL)[a]			
PCC (Manufacturer)	Availability	II	VII	IX	X	C	S	Z	Other
3-Factor									
Uman-Complex D.I. (Kedrian)	Italy	28	<0.1	28	21	9	5	Yes	Low levels of ACF
Bebulin VH (Baxter Healthcare Corp.)[b]	US	24-37	<5	24-37	24-37	NA	NA	No	Heparin added
Profilnine (Grifols)[b]	US	87	NT	69	54	0	0	No	
4-Factor									
Beriplex P/N (CSL Behring)	Canada, Western Europe	20-48	10-25	20-31	22-60	22-31	17-19	Yes	ATIII and heparin added
Kcentra (CSL Behring)	US	Yes[d]	Yes[d]	Yes[d]	Yes[d]	Yes[d]	Yes[d]		
Cofact (Sanquin)	Netherlands, Austria, Belgium, Germany	30	13	23	26	4	21	Yes	ATIII added
Kanokad (LFB-Biomedicaments)	France	14-35	7-20	25	14-35				
Octaplex (Octapharma)	Canada, Western Europe	31	16	22	24	12	24	Yes	Heparin added: low factor VIIa content
Prothromplex Total (Baxter Healthcare Corp.)	Sweden, Germany, Austria	12	11	8	11	4	8	Yes	ATIII and heparin added
Activated PCC									
FEIBA (Baxter Healthcare Corp.)[b]	US	1.3 IU/IU	0.9[c] IU/IU	1.4 IU/IU	1.1 IU/IU	1.1 IU/IU	NA	No	

ACF = anticoagulation factor; AT = antithrombin; NA = not available; NT = nontherapeutic levels; PCC = prothrombin complex concentrate.
[a] After reconstitution.
[b] Bebulin, Profilnine, and FEIBA have received Food and Drug Administration license but are not approved for the reversal of warfarin activity.
[c] An activated factor VII in this product.
[d] Potency of individual factors is labeled on the packaging.

Nitzki-George D, et al. *Ann Pharmacother* 2013;47:841-55.

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Indications/Complications:

Although originally developed to isolate factor IX for the treatment of hemophilia B, use of PCC for this and other isolated, congenital coagulation factor deficiencies has fallen out of favor due to the availability of high-purity, isolated factor concentrates.[2] In the United States, PCCs are currently FDA approved for congenital or acquired deficiency of vitamin K-dependent clotting factors when purified, specific coagulation factor products are not available, and for the urgent reversal of VKA therapy in the setting of life-threatening hemorrhage. Until recently, the vitamin K antagonist warfarin has been the mainstay of treatment for prevention of thromboembolic events.[6] It is used for the prevention of thrombosis and strokes in patients with atrial fibrillation, for patients with prosthetic heart valves, and for the treatment of deep vein thrombosis and pulmonary embolism.[6] The risk of major bleeding with warfarin therapy ranges widely from 0% to 19.3%.[6] Four options exist for reversal of VKA therapy: withholding VKA therapy, administering oral or IV vitamin K, replacing the deficient factors using PCC or fresh frozen plasma (FFP), and bypassing the coagulation cascade with recombinant activated factor VII (rFVIIa).[2]

In the event of life-threatening hemorrhage secondary to VKA therapy or the need for emergency surgical intervention while therapeutic on VKA therapy, withholding VKA therapy or administering IV vitamin K will not reverse the anticoagulation in a timely fashion. Addressing the use of rFVIIa, a 2012 Cochrane review by Simpson and colleagues analyzing twenty-nine randomized control trials found a significantly increased risk of arterial thrombosis when used outside of its licensed indications; VKA reversal is not one of these licensed indications.[7] Thus, when time is of the essence the choice comes down to PCC or FFP.

As commonly occurs in clinical practice, PCCs have been used off-label. With the introduction of direct factor Xa inhibitors and direct thrombin inhibitors, warfarin is no longer the only oral anti-thrombotic agent available. Although reversal agents for direct Xa inhibitors and direct thrombin inhibitors do not exist, PCC has been used in the setting of massive hemorrhage associated with these newer anticoagulants.[3] PCC has also been utilized in massive hemorrhage secondary to trauma unrelated to anticoagulation.[8] In the operating theater, PCC has been employed in coagulation management in both liver transplantation and cardiac surgery.[9, 10] It is likely that off-label uses of PCC will continue to grow.

"Thus, when time is of the essence the choice comes down to PCC or FFP"

Administration of PCC does not come without risks. Complications associated with PCC include thrombosis, allergic reaction, and heparin-induced thrombocytopenia for those preparations containing heparin.[2] Thrombosis is the major adverse event linked to PCC use, including venous thromboembolism, disseminated intravascular coagulation, microvascular thrombosis, myocardial infarction, and thrombotic stroke.[3] In Canada, Hickey and colleagues performed a retrospective cohort study of adverse event frequency following urgent warfarin reversal with 4F-PCC versus plasma in two tertiary care emergency departments. It was conducted as a before-after study over consecutive 2-year periods, with the plasma group consisting of 149 patients enrolled from 2008 to 2010 and the 4F-PCC group consisting of 165 patients enrolled from 2008-2010.[11, 12] The primary outcome was serious adverse events, including death, ischemic stroke, myocardial infarction, heart failure, venous thromboembolism, and peripheral arterial thromboembolism within 7 days. The incidence of serious adverse events was 9.7% for the 4F-PCC group compared with 19.5% for the plasma group (P=0.014; relative risk, 2.0; CI, 1.1-3.5). After adjusting for baseline history and reason for treatment, this remained significant in multivariable regression analysis.[12] It is important to note that this study only evaluated PCC complications in the setting of VKA reversal. Thus, the results cannot be generalized to PCC use in another context. Further studies are necessary to examine the incidence of thrombotic complications associated with PCC use for other indications, such as trauma or surgical coagulopathies.

PCC v Fresh Frozen Plasma:

PCC has many advantages over FFP. Most importantly, PCC corrects the INR more rapidly than FFP.[3] Unlike FFP, which is frozen and must be thawed and then warmed, PCC can be stored at room temperature and is easily prepared by reconstituting the lyophilized powder with diluent.[3] Traditionally, FFP is given in doses around 15 cc/kg. This large amount of volume can have a deleterious effect on a patient with a compromised cardiovascular system, putting the patient at risk for fluid overload, congestive heart failure, and cardiogenic pulmonary edema. In contrast, PCC requires injection volumes of only 1-2 cc/kg because of the high concentration of coagulation factors.[3] The minimal preparation and smaller amount of volume allow for much quicker administration of PCC in urgent situations. Another benefit is the improved infectious safety profile of PCC compared to FFP.[2] While the viral reduction process differs amongst the various PCC agents, these processes are effective at minimizing the risk of infectious transmission of many agents, including prions.[2] A further advantage of PCC is elimination of transfusion-related acute lung injury, which is a major cause of death associated with FFP transfusion.[2]

Recent Data:

Despite the many advantages, PCC is not universally available and its cost can render it prohibitive. In addition, the risk of thrombosis is not yet fully understood. Thus, a careful examination of the data is necessary to justify the use of PCC over FFP. With few exceptions, the majority of the published data suggests that PCC administration results in a significantly faster INR reduction when compared to FFP administration.[13, 14, 15, 16, 17] However, none of these studies are randomized control trials, and all of them use retrospective analysis. The studies are further hindered by a small number of patients and heterogeneity, lacking standardization among composition of PCC, dosing

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regimen of PCC, and concurrent therapy administered.[2] Given the paucity of prospective, randomized data, it is unclear whether the faster reduction in INR seen with PCC translates into improved clinical outcomes.

The newer literature features prospective, randomized control trials that attempt to expand upon earlier, retrospective data. Demeyere and colleagues performed a prospective, randomized trial in Belgium comparing 4-factor PCC to FFP in forty patients on oral anticoagulation therapy with VKAs (INR ≥ 2) undergoing semi-urgent or urgent cardiac surgery. It showed that 15 minutes after cardiopulmonary bypass (CPB), more patients reached the target INR with PCC than with FFP; however, there was no significant difference in mean INR values 60 minutes after CPB.[18] Another randomized control trial was conducted by Sarode and colleagues at 36 centers in the United States and Europe to establish noninferiority of 4F-PCC compared to plasma. The study enrolled 216 VKA-treated patients with acute major bleeding. In addition to IV vitamin K, the patients were randomized to receive either 4F-PCC or FFP. Rapid INR reduction, measured as an INR ≤ 1.3 at 30 minutes, was achieved in 62.2% of the 4F-PCC group compared with 9.6% of the plasma group. In addition to establishing the superiority of 4F-PCC, the study also demonstrated similar rates of adverse events between the groups.[19]

Discussion:

Although widely used in Europe, use of PCC is just now entering into mainstream practice in the United States. The American College of Chest Physicians 2012 edition of antithrombotic guidelines makes a 2C recommendation for 4-Factor PCC administration rather than FFP for rapid reversal of VKA-associated major bleeding with IV vitamin K supplementation.[20] The current evidence strongly supports the fact that PCC produces a more rapid reduction in INR than FFP. However, it fails to answer the more critical question of whether PCC improves clinical outcome. Further studies are warranted to investigate whether PCC confers a mortality benefit over FFP. Likewise, these studies must eliminate the heterogeneity that exists in the current literature by taking into account the different PCC products available. The clotting factor and anticoagulant composition of each PCC varies by brand, and it is crucial to determine the appropriate dosing regimen for each brand in order to ensure both beneficial and safe outcomes.

Although widely used in Europe, use of PCC is just now entering into mainstream practice in the United States.

With greater availability have come promising off-label uses of PCC to treat life-threatening hemorrhage secondary to direct thrombin inhibitors and direct factor Xa inhibitors and to act as a substitute for FFP in the setting of life-threatening hemorrhage unrelated to anticoagulants.[21] The European Society of Anaesthesiology's 2013 guideline for the management of severe perioperative bleeding includes a 2C recommendation for the use of PCC, FEIBA, or rFVIIa as non-specific antagonists for patients on direct Xa inhibitors or direct thrombin inhibitors with life-threatening hemorrhage or intracranial hemorrhage.[2] As evidenced by the 2C recommendation, human data on reversal of hemorrhage associated with direct Xa inhibitors and direct thrombin inhibitors is sparse, consisting mostly of case reports and in-vivo/ex-vivo studies in healthy volunteers.[23, 24, 25, 26, 27, 28, 29, 30, 31] The majority of the case reports did not have favorable outcomes.[23, 24, 25, 26, 27] However, the ex-vivo and in-vivo studies showed more promising results.[28, 29, 30] In a clinical review of the literature by Lazo-Langner and colleagues, the best available evidence suggests PCC, either activated or inactivated, might be the best option currently available for reversing the new anticoagulants.[31] Furthermore, both laboratory and human studies suggest that PCC might correct bleeding and reverse the effects of rivaroxaban, a direct factor Xa inhibitor, better than dabigatran, a direct thrombin inhibitor.[31] In the trauma arena, a handful of retrospective analyses suggest that PCC may be beneficial in treating trauma-induced coagulopathy.[8, 32, 33, 34] In an observational study, Schochl and colleagues set out to investigate the impact of PCC in trauma-induced coagulopathy via measurement of laboratory data relating to thrombin generation. The data showed increased endogenous thrombin potential and decreased antithrombin concentrations associated with PCC, implying a potential pro-thrombotic state that was not reflected by standard coagulation tests.[34] This implies that PCC may intensify the pro-thrombotic state that already exists in the trauma patient, possibly leading to devastating thrombotic complications. As with trauma patients, surgical patients have a heightened pro-thrombotic state secondary to the hemostatic derangements induced by surgical manipulation. Retrospective studies have examined the use of PCC in the surgical population, including the subsets of cardiac surgery and liver transplantation.[9, 10, 35, 36]

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Photo credited by Hawaii Tourism Authority (HTA) Tor Johnson

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Overall, the trend in these studies is that PCC achieves adequate hemostasis in the face of severe bleeding and decreases the use of blood products without a significantly increased incidence of thrombotic events.[9, 10, 35, 36] While this retrospective data is encouraging, large, randomized control trials are necessary to delineate the appropriate clinical circumstances in which PCC should be utilized. PCCs have become an indispensable tool in the management of urgent reversal of VKA therapy. In the future, PCC use will likely expand well beyond this realm.

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Whither EGDT for Sepsis?

Jordan E. Brand, MD
Staff Anesthesiologist
San Francisco Veterans Affairs
Medical Center, UCSF
San Francisco, California

Most clinical trials provide fodder for further research; a smaller number result in changes in practice. Still rarer are the studies that produce a "paradigm shift" in care, a durable (and sudden) change in the way clinicians think and manage patients. Such studies can have unpredictable effects, often benefitting patients, but also making further research more difficult by changing what is considered the standard of care and, indeed, what is considered ethically permissible to study at all.

In 2001, one such paradigm shift occurred when early goal-directed therapy (EGDT) for sepsis and septic shock rose to favor, largely due to a study by Rivers et al. published in the New England Journal of Medicine (NEJM).[1] In this study, 263 patients with severe sepsis or septic shock were randomized to receive either standard care (with some suggestions for resuscitation goals) or care via a detailed protocol designed to optimize tissue oxygenation. A major intervention in the protocol group was the placement of a central venous catheter (CVC) that measured central venous oxygen saturation (ScvO2) and helped guide administration of fluids, transfusions, and inotropes. These treatments were administered in a special unit of the emergency room until the patients could be admitted to the ICU. Patients treated with EGDT exhibited better indices of perfusion and had a 16% absolute decrease in hospital mortality. This study brought a great deal of attention to the early resuscitative period in sepsis and has influenced both clinical guidelines and practice.[2]

Despite the huge impact of the 2001 Rivers EGDT study, its findings were not re-evaluated until recently. In May 2014, a follow-up study, called ProCESS, appeared in NEJM. The ProCESS trial was designed to test which of three approaches to early resuscitation in sepsis was the best: the "Rivers" EGDT protocol (referred to as "protocol-based EGDT"), an alternative protocol that focused on specific goals but did not rely on central venous catheterization or ScvO2 monitoring (referred to as "protocol-based standard therapy"), or usual care at the direction of bedside physicians without application of a specific protocol.[3] Treatments were administered for the initial 6 hours of resuscitation after enrollment and randomization. 1341 patients were enrolled from 31 emergency departments across the United States. Patients in the group receiving protocol-based EGDT, unsurprisingly, were much more likely to have a CVC placed, as well as to have ScvO2 measured, and received more inotropes and blood transfusions than either of the other groups. While the group receiving usual care received the lowest amount of IV fluids in the first 6 hours of treatment, the protocol-based standard therapy group actually received the most. There were no significant differences between the groups in 90-day or 1-year mortality or rates of organ failure. Notably, the ProCESS trial used a lower transfusion threshold (Hgb < 7.5 mg/dL) and had a slightly higher rate of antibiotic administration in the first 6 hours than the 2001 Rivers trial.

Close on the heels of the ProCESS trial, October 2014 saw the publication of the ARISE study, which compared EGDT (based on the 2001 Rivers protocol) to usual care in patients with early septic shock. This study enrolled 1600 patients from centers in Australia, New Zealand, and a few other international locations, none in the United States.[4] Similarly to ProCESS, ARISE showed no difference in in-hospital mortality, length of hospital stay, or duration of organ support between the groups. The EGDT group received significantly more blood transfusions, more inotropes, and more fluids (although the difference in volume administered between the

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Whither EGDT for Sepsis?

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groups- less than 200 mL- does not seem clinically important). Patients in the EGDT group were also more likely to have a CVC or arterial catheter placed and to have ScvO2 monitored. Antimicrobials were administered early, usually within the first two hours after presentation to the ED.

So how are we to interpret the results of these three trials? There are several reasons why ProCESS and ARISE might have found different results than the original Rivers study. First, both recent trials were much larger than the 2001 study and enrolled patients from multiple centers; smaller, single-center trials are known to be at greater risk of incorporating biases and consequently exaggerating effect sizes.[5] Another difference is found in mortality rates: the original Rivers study found 60-day mortality of 56.9% in the standard-care group and 44.3% in the EGDT group, numbers which are more than twice those of either 2014 study. This is despite the fact that APACHE II scores were similar in the Rivers trial and the ProCESS trial and only slightly lower in ARISE. It may be that EGDT is a victim of its own success: sepsis mortality has been decreasing over time,[6] and it may be that some of this change is due to the broader adoption of EGDT. Making "usual care" closer to what the EGDT group received in the 2001 Rivers study. Because EGDT is composed of multiple interventions, some of which have certainly influenced critical care practice, it is harder to identify effects of EGDT as a whole. This is supported by the fact that the differences in fluid administration between groups in ProCESS and ARISE were substantially smaller than the inter-group differences in the Rivers trial.

It does seem that intensivists should no longer feel an obligation to routinely institute the more aggressive parts of the Rivers protocol, such as ScvO2 monitoring, dobutamine infusion, or transfusion of PRBCs, unless they are warranted by the specific clinical situation. Indeed, using surrogates such as arterial lactate clearance to guide resuscitation has been shown to be equally effective as using ScvO2.[7] However, this does not mean that we should abandon our focus on goals in the initial phase of sepsis resuscitation. While some liberalization of critical care practice is probably in order, it would be counterproductive to abandon valuable techniques that, for many if not most intensivists, are already part of our standard of care.

One problem particularly common in paradigm shifts occurs when they are seized upon by non-medical actors such as politicians. In response to the high-profile death of a 12-year-old boy from septic shock, New York has now mandated that all hospitals in the state adopt protocols for early diagnosis and treatment of sepsis and that adherence and outcomes must be reported to the state Board of Health; there is evidence that such plans may be implemented in other states or nationally in the future.[8] Unfortunately, this effort may cause hospitals to craft protocols based on a too-strict emulation of the Rivers methodology, and may also cause their care to be judged based on practices that are no longer considered optimal.

As ProCESS and ARISE have highlighted, our understanding of sepsis and how to best treat it is imperfect, and we must be careful here, as in other areas of medicine, not to enact strict regulations that will prevent medical practice from evolving in step with the best evidence.

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Nominating Committee Candidate Announcement

Candidate for Board of Directors: Laureen L. Hill, M.D., M.B.A.

Dr. Hill is Professor and Chair of Anesthesiology at Emory University School of Medicine in Atlanta, Georgia where in addition to her administrative duties she continues a busy clinical practice in preoperative medicine, intraoperative anesthesiology and critical care medicine. She is a strong advocate for anesthesiologists as the ultimate peri-operative physicians and she is an ardent proponent of multidisciplinary critical care. Dr. Hill has been a longstanding member of SOCCA serving on the education committee, contributing as a mentor for the resident section at the annual meeting and previously working as program co-chair of the annual meeting for three consecutive years. She was elected to the Board of Directors and is completing a three year term.

Dr. Hill acknowledges the many pressures we face including increasing clinical care demands, inadequate workforce, organizational and professional reimbursement pressures and changing practice models for critical care services. She strongly believes our future relevance and success as anesthesiologist intensivists depends on our ability to effectively demonstrate our value across the care continuum, embrace evolving information technologies to standardize and manage the care environment, train our physicians to excel as leaders of team-based care in and out of the operating room and invest significantly in innovation and discovery.

Dr. Hill would be privileged to serve this Society and its membership and is seeking re-election for a seat on the Board of Directors.

Candidate for Board of Directors: Mark E. Nunnally, M.D., FCCM

Dr. Nunnally received his undergraduate degree in Spanish and his M.D. at the University of Washington. He completed his residency at the University of Chicago, where he was a chief resident. His fellowship in Critical Care Medicine was at the University of Pennsylvania. He returned to join the faculty at the University of Chicago, where he is currently an Associate Professor. He divides his clinical time between the operating rooms and the intensive care unit.

Dr. Nunnally's academic interests are divided between teaching and research. His involvement in resident education includes directing the departmental journal club, lecturing on a variety of ICU and OR related topics, and regular clinical teaching activities. He is the critical care fellowship program director for his department. Dr. Nunnally's research interests concern the role of technology in patient safety. His work to date has focused on infusion devices, delivery systems, incident reporting, and most recently medication reconciliation. He is a consultant in GRADE methodology for rating evidence and translating it into recommendations.

Dr. Nunnally's leadership experience includes membership on multiple committees, including the evidence methodology group for the Surviving Sepsis Campaign, chairman of the American Society of Anesthesiologists' Committee on Critical Care Medicine. He has served the last three years as a director for SOCCA, and hopes to continue to serve the society in this role. He sees the current environment a ripe one for anesthesiology intensivists, believing in the value of critical care. Anesthesiology practices, hospitals and those who finance them can see value here more than ever before. Critical care can be the centerpiece of anesthesiology training. Opportunities to discover new knowledge abound in the ICU environment.

In addition, Dr. Nunnally is an oral examiner for the American Board of Anesthesiology. Outside of work, his interests include international travel, baseball, architecture and urban design, jazz music, and cooking. He is a beer and wine enthusiast and a would-be gourmand. He is passionate about the role of Anesthesiologists in critical care medicine and interested in continuing to build interest in the subspecialty.

The SOCCA Nominating Committee will present the following slate of candidates to the SOCCA membership during the Society's Annual Membership Business Meeting on Friday, March 20, 2015, 5:00-5:45 pm, at the SOCCA 28th Annual Meeting and Critical Care Update at the Hilton Hawaiian Village Resort, Honolulu, Hawaii.

Electronic voting will be available beginning Thursday, March 19 and will end on Friday, March 20 at 5:20 pm Hawaiian time. Elected Directors will be announced at the end of the Business Meeting, at 5:45 pm. Information regarding the electronic voting will be emailed to members prior to the Annual Meeting.

SOCCA members will vote to elect two (2) Board of Directors (for a 3-year term). The terms will begin March 2015.

Board of Directors:
Laureen L. Hill, M.D., M.B.A.
Mark E. Nunnally, M.D., FCCM

Fellowship Review: The Critical Care Fellowship of the Department of Anesthesiology at the Medical College of Wisconsin

Brian A. Fischer, MD, PhD
Assistant Professor of Anesthesiology
Medical College of Wisconsin
Milwaukee, Wisconsin

The Department of Anesthesiology at the Medical College of Wisconsin (MCW) offers an exciting and rewarding fellowship in Critical Care Medicine. The program provides the fellow with multiple opportunities to hone their diagnostic skills on challenging patients from multiple disciplines, with the goal of becoming an expert and leader in Critical Care.

MCW fellows rotate through a variety of Intensive Care Units (ICU), each with its own unique set of high acuity patients requiring challenging medical decision-making. The ICUs are located in two hospitals - Froedtert Memorial Lutheran Hospital and the Clement J. Zablocki Veteran's Affairs Hospital. Froedtert Hospital is a Level 1 Trauma Tertiary Care Hospital with 500 beds and the only teaching hospital in Southeastern Wisconsin. The Clement J. Zablocki VA Hospital, with just over 150 beds, offers a full range of surgical specialties including both neurosurgery and cardiothoracic surgery. The Department of Anesthesiology has directorship of two primary ICU locations: the Cardiovascular Intensive Care Unit (CVICU) at Froedtert Hospital and the VA-Surgical Intensive Care Unit.

The Froedtert CVICU is a twenty-bed facility for cardiothoracic and vascular surgery patients as well as cardiology patients. The Anesthesiology CVICU team primarily manages the critical care issues for the cardiothoracic and vascular surgery teams, but also provides consultation for ventilator and induced hypothermia management of cardiac patients. The cardiothoracic surgeons provide care including coronary artery bypasses (CABG), valve replacements, extracorporeal membrane oxygenation (ECMO), left ventricular assist devices (LVAD) and heart transplants as well as other cardiothoracic surgical procedures. The vascular surgery team performs a wide variety of arterial bypass procedures, repairs abdominal aortic aneurysms and jointly treats thoracic aortic aneurysms with the cardiothoracic surgery team. The fellows have the opportunity to manage these patients with a multidisciplinary team consisting of both residents and nurse practitioners overseen by a staff critical care anesthesiologist working in conjunction with the surgical teams.

The VA-ICU is an 18 bed facility for critically ill medical and surgical patients. The Surgical Intensive Care Unit (SICU) service cares for patients across the spectrum of the surgical specialties offered at the VA Hospital. Here, the Anesthesiology/Critical Care fellow leads the critical care team on teaching rounds and coordinates care, as well as teaches in didactic discussions. The VA-SICU team also offers consultative services for medical patients.

A further SICU experience is offered in the SICU at Froedtert Hospital, allowing fellows to treat all surgical patients not cared for in the CVICU. Patients include challenging Level 1 trauma patients, liver transplant patients, and general surgical critical care patients. The unit is staffed by surgical critical care physicians, and the team consists of residents from the departments of Surgery and Emergency Medicine. This rotation provides the fellow with a unique opportunity to be a leader of a multidisciplinary critical care team.

The medical intensive care unit (MICU) experience allows the fellow to care for critically ill medical patients as well as learn principles of ICU management and patient triage across the hospital. The anesthesiology critical care fellow serves as MICU triage physician for patients in the Emergency Department and provides consultative services for patients admitted to non-ICU areas.

The Neurocritical Care Unit (NICU) is utilized by both the neurosurgical and neurology services. The neurosurgical patients include those recovering from intracranial procedures for seizures as well as tumors and vascular procedures. Neurology patients include those with seizure disorders, those undergoing neuro-interventional procedures, stroke patients, and those with more obscure neurological diagnoses. The NICU is staffed by Neuro-critical care physicians, giving the Anesthesiology Critical Care fellow a rich environment to learn the nuances of caring for patients with complex neurological pathology.

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Fellowship Review: The Critical Care Fellowship of the Department of Anesthesiology at the Medical College of Wisconsin

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The Anesthesiology Critical Care fellowship at MCW offers a rich, multidisciplinary learning curriculum. The year begins with a lecture series concentrating on basic critical care topics and in-depth ventilator management during the first two months of the fellowship. Much of this introductory material is taught by Pulmonary Critical Care faculty. Also, the CVICU offers a year-long multidisciplinary conference series concentrating on the management of surgical critical illness as well as topics in ethics, palliative care, and echocardiography. The VA-ICU presents multiple teaching opportunities for the fellow in the form of three conferences each week done jointly with the Pulmonary/Critical Care faculty, a journal club led by the fellow, case presentations, and other attending staff lectures and discussions. Fellows are also provided opportunities to participate in department-wide teaching conferences and committees.

All fellows attend the Fundamental Critical Care Support (FCCS) course and are expected to become instructors for it. A year-long focused fellow lecture series on such topics as the use of ultrasonography in the ICU is given by attendings and fellows from multiple disciplines. Furthermore, TEE training can be obtained via simulator as well as on patients who are undergoing cardiac procedures in the operating room and CVICU. Opportunities are plentiful for the fellow to be involved in simulator training for the residents allowing the fellows to have a hands-on experience in medical simulation from both the learner and instructor viewpoints.

Multiple two to four week research electives are offered in the fellowship. For those interested in further research opportunities, a second research year can be added to the fellowship, pending approval from the program director, Dr. Sylvia Dolinski.

Milwaukee is a vibrant city of approximately 600,000 people located on Lake Michigan approximately 90 miles north of Chicago. Summers are packed with festivals ranging from Irish Fest to German Fest to Bastille Day, to name a few. The most popular of these events is Summerfest – a city-wide music celebration spanning a week each July. Milwaukee also is home to several professional sports teams. Outdoor activities abound, such as biking, hiking and water sports on a Lake Michigan. Those seeking other cultural venues will be pleased to know that Milwaukee has a renowned symphony orchestra, an opera company, and is host to top musical and stage performances throughout the year. Its art museum is world famous, both for its collections and its magnificent pavilion designed by Santiago Calatrava.

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