MESSAGE FROM THE CHAIR
Karen J. McAllen, PharmD, FCCM

I hope everyone has had a safe, enjoyable summer, particularly those in the North who endured the “Polar Vortex” this winter. Now that we are into football season, some of us have already been disappointed, while others are still remaining hopeful that their team continues to be productive.

Speaking of productive, the CPP Section has been busy working on a number of initiatives. Many of these initiatives are highlighted in the committee sections of this newsletter. For those of you looking at becoming board certified for critical care in the upcoming years, SCCM and the CPP Section are looking at how we can support you in this endeavor. Good luck to those of you taking the exam in October 2015.

I hope many of you are able to attend the Annual Congress in Phoenix, Arizona, in January. Again, there will be many sessions that may pique your interest. The CPP Section is happy to provide a symposium prior to the start of the meeting. This session, “How to Develop or Enhance Your ICU Practice,” will take place on Saturday, January 17 from 2 to 4 PM. Following will be a new attendees orientation/meeting, which will precede the member reception. If you are aware of anyone who is attending Congress for the first time, please encourage them to attend as this is always a good way to learn how to become more involved in SCCM and the CPP Section, as well as being an opportunity to meet both seasoned and new members. Again this year, the CPP Section will be supporting a recruitment exchange at Congress. It will occur just before the section business meeting.

The SCCM Program Committee is also working hard on developing the full-day pre-Congress education session, “Critical Care Pharmacotherapy: Challenges and Controversies” to be held on Saturday, January 17. This is always an innovative, informative session, and we are fortunate to have a full day devoted for this excellent programming.
The topics this year are relevant to many areas of critical care practice and will give you excellent tools for managing our complex patients and medical issues. There is an additional charge for this session but always well worth it.

As always, if you have input or ideas for the CPP Section, I would like to hear from you. Please contact me at Karen.mcallen@sanofi.com.

**CPP COMMITTEE CORNER**

**Communications Committee**
*Deepali Dixit, PharmD (Chair), and Simon Lam, PharmD (Chair-Elect)*

*Abstracts for Congress 2015*

The Communications Committee once again will be compiling a list of CPP Section members whose abstracts were accepted for presentation at the 2015 Annual Congress. This list will be included in the December newsletter. If you are a co-author on an abstract but the submitting author is not a CPP Section member, please forward the accepted abstract number, title, and complete author list to Simon Lam (lams@ccf.org). This will help ensure that we publish the most complete list of CPP Section members with accepted abstracts.

Additionally, the December newsletter will include a summary of CPP Section meeting schedule and CPP members involved in educational sessions at this year’s Congress in Phoenix, Arizona.

If you have any questions regarding membership in the Communications Committee or contributions you would like to make to the CPP Section newsletter, please contact Deepali Dixit (deepali0420@gmail.com) or Simon Lam (lams@ccf.org).

**Education Committee**
*Jorie Frasiolas, PharmD (Chair), and Jeff Gonzales, PharmD (Chair-Elect)*

The CPP Education Committee continues to partner with the Society on several key initiatives, including educational modules, a toolkit for protocol implementation, education for board recertification in critical care pharmacotherapy, electronic posters, and Journal Club.

A webcast on spontaneous awakening trials and spontaneous breathing trials will take place in quarter four of 2014. An email announcement will be distributed with additional information.

Electronic posters presented at the 2014 SCCM Annual Congress are available in the CPP Section iRoom and LearnICU eCommunity. To view the posters in the iRoom, please access the committee documents along the left-hand menu. The posters can also be found in the LearnICU eCommunity at [http://community.sccm.org/p/fo/si/topic=47](http://community.sccm.org/p/fo/si/topic=47) or by visiting the LearnICU Pharmacology Knowledge Area.

Journal Club continues to be held the third Friday of every month at 2 PM ET. Upcoming dates include October 17, November 21, and December 19. If you would like to receive the monthly notification and link to access the session, please contact Karen Berger at karenberger7@gmail.com or sccmcppjc@gmail.com.
Membership Committee
Laura Aykroyd, PharmD (Chair), and John Allen, PharmD (Chair-elect)

Mentor-Mentee Program

The Mentor-Mentee Program was developed to provide pharmacist members of the CPP Section with guidance in a variety of different areas such as clinical practice, career advancement and teaching. All members of the CPP Section are eligible to participate in the program in either a mentor or mentee capacity.

The Membership Committee is actively seeking CPP members who are interested in serving as a mentor. In recent months, we have had a tremendous number of people seeking mentorship. While the number of requests is a testament to the success of the program, there have been times when it has been difficult to find suitable matches for the mentees. We are in need of mentors in all areas of critical care, but particularly in areas such as emergency medicine to support the growing number of pharmacists in this field.

Members interested in being mentored are encouraged to contact us as soon as possible. Mentorship is available to all CPP members regardless of whether you are a new practitioner looking to get started in a new career or a more experienced pharmacist looking to advance your career outside of the clinical arena. If you would like more information regarding the program or would like to participate, please email either Laura Aykroyd (laykroyd@iuhealth.org) or John Allen (johnallen@health.usf.edu). We look forward to working with our current and prospective mentors and mentees and for the continued success of this program.

Free Memberships for Pharmacy Trainees

SCCM offers sponsored memberships to critical care, nutrition, and emergency medicine pharmacy residents and fellows. If you are the director of one of these pharmacy training programs and did not receive information about sponsored memberships for your trainees, please contact Laura Aykroyd (laykroyd@iuhealth.org) or SCCM at sponsoredmembership@sccm.org for information.

Patient Safety Committee
Lisa Harinstein, PharmD (Chair), and Elizabeth Sinclair, PharmD (Chair-Elect)

Thank you to those members who submitted applications for the 2014 CPP Patient Safety Awards. Submissions are under review and the winners will be announced at the 2015 Annual Congress CPP Section business meeting.

Additionally, members of the Patient Safety Committee continue to work on a retrospective study examining medication-related admissions to the ICU. Additional participation is still needed on the project. If you are interested in getting involved, please email Jaclyn Leblanc (jaclynleblanc@hotmail.com) or Lisa Harinstein (harinsl@ccf.org). Lastly, the Patient Safety Committee has contributed to the development of a pamphlet highlighting key points in the treatment of sepsis. The pamphlet is produced in collaboration with the SCCM Patient and Family Support Committee.

Program Committee
Moo Sultan, PharmD (Chair), and Marilyn Bulloch, PharmD (Chair-Elect)

The CPP Program Committee has been coming together to complete the charges for the year. As mentioned before, the committee has decided on the topics and speakers for the Congress session, Year in Review: Pharmacy. This year’s topics will be fluid resuscitation, burns, and infectious disease in critically ill. At the end of the month, the speakers will be contacted by previous speakers who can offer guidance and a helpful document developed by the committee.

The committee is also planning for pre-Congress symposium, member reception, and Recruitment Exchange. The pre-Congress symposium programming ideas are being reviewed by the Steering Committee, and the date has been finalized as Saturday, January 17, 2015, from 2:00 to 4:00 PM. We learned a lot from the Recruitment Exchange this past year and are working on making it a successful event benefiting both employers and job seekers. If anyone has any suggestions for the Recruitment Exchange or the pre-Congress symposium, please let me know. Finally, the Visiting Clinical Professor Program is excited to send Stephanie Mallow-Corbett to Vidant Medical Center this fall. More updates on the visit to come in the near future.

If you have any questions or suggestions, please email Moo Sultan (smsultan@unch.unc.edu) or Marilyn Bulloch (novellm@gmail.com)

Research Committee
Erin Frazee, PharmD (Chair), and Mitch Daley, PharmD (Chair-Elect)

The CPP Research Committee is well into the year with exciting updates for services and resources available to you. One of the greatest strides this committee has made this year is further developing how the committee can better support your research!

- Are you early in the research process and looking for grant funding opportunities? In the iRoom under Non-SCCM Funding, you can find a list of potential funding opportunities from multiple sources (pharmacy foundation, pharmacy industry, private foundations, and federal funding).
- Are you having difficulty optimizing your methodology or analytical plan and need to consult an expert? Utilize the Research Consult Service by emailing your inquiry to cpppresearchconsult@gmail.com. Committee members will identify an expert who will work with you to get the one-on-one feedback you need.
- Are you seeking feedback for your manuscript, grant proposal, CCPTN research proposal or CPP documents? The CPP Research Peer Pre-Review Service can locate experts to provide a peer-review prior to a formal submission. Email the CPP Research Chair (Erin Frazee at Frazee.Erin@mayo.edu) or Chair-Elect (Mitch Daley at mjdaley@seton.org) to submit your request.

In addition, the CPP Research Committee continues to review more than 20 journals to identify primary literature relevant to the critical care practitioner. On a monthly basis, the Critical Care Pharmacotherapy Literature Updates (CCPLU) team provides readers with a concise review of relevant research in abstract form and shares insights on practice implications to keep you up to date in the field of critical care and pharmacotherapy. The value of such a service will now be recognized in its second publication as a Special Feature in the American Journal of Health-System Pharmacy.
If you would like further information about any of these activities or would like to get involved in the Research Committee, please contact Erin Frazee (frazee.erin@mayo.edu) or Mitch Daley (mjdaley@seton.org).

Pharmacotherapy Article

Summary of the reversal options for the novel oral anticoagulants in life threatening bleeding
Kimberly Berger, PharmD, BCPS

Anticoagulation plays a prevalent role in today’s medicine. An estimated 2 million people suffer from venous thromboembolism in the United States each year. Additionally, the risk of ischemic stroke in patients with atrial fibrillation (AF) is approximately 5% per year. Anticoagulation has proven effective in both reducing the risk and treating thromboembolism. However, the use of anticoagulation is not without significant bleeding risks.

Prior to 2010, the options for thromboembolic disease and stroke prevention were limited to warfarin and parenteral anticoagulants such as the heparin products, fondaparinux, and the direct thrombin inhibitors. Warfarin, a vitamin K antagonist, has long been the mainstay of oral anticoagulant therapy. However, limitations with its use include frequent international normalized ratio (INR) monitoring, variable dosing, drug-drug and drug-food interactions, and the role of genetics in dosing. These limitations and lack of oral options led to the development and approval of different classes of oral agents. These agents exert their effects by inhibiting factors within the clotting cascade. Dabigatran, a direct thrombin inhibitor, was approved for use in nonvalvular AF to prevent stroke and systemic embolism. Rivaroxaban and apixaban, both anti-Xa inhibitors, are the other oral anticoagulants on the market. Both have approved indications for nonvalvular AF for prevention of stroke and systemic thromboembolism, treatment of deep vein thrombosis and pulmonary embolism, and prophylaxis following hip and knee arthroplasties. The benefits of these agents over warfarin include a quick onset of anticoagulant effect which requires no bridging therapy and the lack of monitoring required with these agents.

Still, a significant bleeding risk is associated with these new oral anticoagulant therapies. In initial approval studies, the bleeding rates of each of these agents were either non-inferior or superior to warfarin. In the RE-LY study, the rate of major bleeding for dabigatran was 3.11% compared to warfarin at 3.36% (P=0.31); however, rates of life-threatening bleeding and intracranial hemorrhage (ICH) were lower with dabigatran than warfarin. In the ROCKET-AF trial, similar results were found for rivaroxaban; the incidence of major bleeding was 3.6% in rivaroxaban group compared to 3.4% in warfarin group (P=0.58), and the incidence of ICH was lower in rivaroxaban group compared to warfarin group (0.5% vs 0.7%; P=0.02). In ARISTOTLE, apixaban had a major bleeding rate superior to that of warfarin (2.13% vs 3.09%; P<0.001), and the rate of ICH was lower than in the warfarin group (0.33% vs 0.8%; P<0.001).

Despite the benefits of these agents and comparable (or lower) bleeding rates for the newer agents, there is still controversy in clinical practice surrounding their use. A high mortality rate is associated with ICH and anticoagulation use, as well as other life-threatening bleeding. In the emergency setting, the challenge surrounds the lack of monitoring to correlate to therapeutic anticoagulation and the lack of well-studied, commercially available reversal options.
The effect of each of these agents on clinical monitoring parameters is not fully understood, which provides a challenge when a patient presents with life-threatening bleeding and the reversal of these agents is considered. With warfarin, the degree of anticoagulation is measured by prothrombin time (PT) and INR. The new agents may have some effect on other markers of anticoagulation, such as activated partial thromboplastin time (aPTT), PT, or ecarin clotting time (ECT). Dabigatran prolongs aPTT, and reversal should be considered if the level is increased as this indicates presence of drug, though it is not well correlated with therapeutic levels. Dabigatran also prolongs ECT, a specific assay for thrombin generation that is not readily available in clinical settings. Rivaroxaban and apixaban have been shown to prolong the PT in a dose-dependent fashion, but a prolonged PT may not be detected at therapeutic doses. There is potential for the use of anti-Xa levels, but the available assays must be calibrated within specific laboratories and this test is also not readily available in clinical settings. Due to these limitations, it is best to rely on the timing of the last dose before the traumatic event and to use clinical judgment when assessing the need for reversal.

In addition to the lack of readily available monitoring, the reversal options for these agents are limited. With warfarin, vitamin K, fresh frozen plasma (FFP), recombinant factor VIIa, and prothrombin complex concentrates (PCC) have all been well studied for INR reversal. Data are limited on the reversal of these new agents. The CHEST guidelines give minimal guidance for the reversal strategies for the new oral anticoagulants in settings of major or life-threatening bleeding, likely due to lack of data. The authors do note that drug administration should be stopped, blood replacement should be given, and local measures should used to stop bleeding. FFP is one blood product that is frequently administered in warfarin reversal. FFP contains small amounts of factors II, VII, IX, and X and has been shown effective in reversing INR. No human studies have looked at FFP use in the reversal of the new oral anticoagulants. The authors of the CHEST guidelines note that FFP is unlikely to influence the effects of these new anticoagulants and that it should only be administered in the setting of dilutional coagulopathy. In most instances, FFP administration will be reserved for mild or moderate bleeding.

Recombinant factor VIIa, (NovoSeven®), which activates the extrinsic pathway of clotting cascade, has previously played a role in reversal of warfarin and has not been well studied in setting of new oral anticoagulants. However, with the introduction of PCCs into the market, recombinant factor VIIa has fallen out of favor for use in warfarin reversal and has a limited role in the reversal of oral anti-Xa inhibitors and dabigatran.

The most promising area of study is surrounding PCC use in anticoagulation reversal. PCCs are derived from human plasma and contain concentrations of nonactivated factors II, VII, IX, and X. Multiple formulations exist including three-factor and four-factor products. The four-factor products contain concentrations of factor VII and the three-factor products do not. Until recently, no four-factor product was available in the United States; Kcentra® was approved in 2013 for use in warfarin reversal. A similar product that was being used before the Kcentra® approval was FEIBA®, which is approved for use in the hemophilic population and contains nonactivated factors II, IX and X and activated factor VIIa.

One benefit of PCCs over other reversal strategies is that they exert their reversal action quickly. They can be infused rapidly and are low volume compared to other options, such as FFP. Pabinger et al evaluated INR reversal in the emergency setting. At 30 minutes after PCC infusion, the INR was reversed to <1.3 in 93% of study group and to 1.4 in 7% (n=43). PCCs also have been evaluated in animal models for the reversal of dabigatran and rivaroxaban. Perzborn et al evaluated the reversal of rivaroxaban in rat models. A four-factor PCC dose of 50 units/kg partially reversed the PT prolongation and shortened mesenteric bleeding time.
Eerenberg et al conducted a prospective, randomized, placebo-controlled crossover study in healthy men to assess the reversal effect of PCCs after anticoagulant administration. A four-factor PCC product (50 units/kg) was used and participants received dabigatran or rivaroxaban. A total of 12 volunteers participated in study. Rivaroxaban induced a significantly prolonged PT of 15.8 ± 1.3 seconds (compared to 12.3 ± 0.7 seconds at baseline). After PCC administration, the PT was completely reversed to 12.8 ± 1.0 seconds, which was statistically significant (P<0.001). Comparatively, dabigatran increased the aPTT to 59.4 ± 15.8 seconds from 33.6 ± 3.3 seconds, but PCC administration had no effect on reversing this coagulation marker. Likewise, dabigatran increased the ECT but PCCs had no effect on ECT reversal. This indicates that four-factor PCC products likely reverse the effects of the oral anti-Xa inhibitors, but it is uncertain whether dabigatran is reversed using this product. FEIBA® may be a better option for the reversal of this agent because it contains the activated form of factor VIIa, but there is a paucity of data in this area.

While the options for the reversal of these agents are limited, the use of PCCs is not without risks. First, there is a thromboembolic risk associated with these agents as they contain high concentrations of specific clotting factors. Clinicians must weigh the associated risks and benefits when determining the need for reversal. FFP should not be administered concomitantly with these agents as this increases the thromboembolic risk. Second, Kcentra®, the four-factor PCC available in the United States, contains heparin, so it is contraindicated in patients with history of heparin-induced thrombocytopenia; FEIBA® is the alternative agent of choice. Obtaining this history in the emergency setting may be difficult, so again risks versus benefits must be weighed. Lastly, the administration of these agents is associated with high costs and thus the availability of these agents may be limited.

In summary, the introduction of new options for oral anticoagulation the past few years has been surrounded by controversy and has presented the critical care setting with a number of challenges. Developing institutional standards and protocols for severe or life-threatening bleeding is strongly encouraged. The use of four-factor PCCs (Kcentra®) at a dose of 50 units/kg is the most widely studied reversal option, although data are limited and many of the reversal strategies are extrapolated from warfarin reversal. When presented with a patient with life-threatening bleeding in emergency setting, clinicians must consider the timing of the last dose if possible, coagulation marker abnormalities, and risks versus benefits of the administration of PCCs.

References:


**CPP Member Spotlight**

*by Drayton Hammond, PharmD, MBA, BCPS*

**April Miller Quidley, PharmD, BCPS, FCCM**

**Critical Care Clinical Specialist**

April Miller Quidley is an adult critical care clinical pharmacy specialist at Vidant Medical Center (formerly Pitt County Memorial Hospital) in Greenville, NC. Vidant Medical Center is tertiary referral center, level 1 trauma center, and one of four academic medical centers in North Carolina. April began practicing in the cardiothoracic surgery ICU in 2012. She has been a preceptor for the University of North Carolina Eshelman School of Pharmacy since 2013.

April has served in leadership positions for the Society of Critical Care Medicine in the Clinical Pharmacy and Pharmacology Section and the American College of Clinical Pharmacy for the overall organization and the Critical Care Practice and Research Network. After first meeting April, you can easily recognize that she is an exceptionally professional,
driven, and gifted critical care pharmacist. Her desire to better the care patients receive at Vidant is evident through her involvement in multidisciplinary committees and healthcare teams. She passes this outlook on to her students and especially her residents. April has been the PGY2 Critical Care Residency Program Director at Vidant since 2013. Her ability to help residents make the most of their time at Vidant can be seen through the various publications and presentations her residents have produced in her two years at the medical center.

April completed her pharmacy education at the University of North Carolina Eshelman College of Pharmacy, where she became interested in the care pharmacists can provide for critically ill patients. She completed a PGY1 and PGY2 critical care residency at University of Kentucky HealthCare and was the chief resident during her PGY2 year. She obtained her BCPS certification after finishing her residencies and plans to sit for the critical care certification exam in 2015. Before moving back to North Carolina, April was a critical care pharmacy specialist at Palmetto Health Richland and a clinical assistant professor at the South Carolina College of Pharmacy for 5 years. She was intimately involved with the preparation of pharmacy students and residents for their careers and appeared on publications or professional posters with more than 60 of these colleagues during her time in South Carolina. April is especially proud of the paths many of her former students and residents have taken; many consistently thank her for the time and dedication she put toward the early stages of their careers.

April remains actively involved in research with residents and colleagues around the country. Her current research interests include acute kidney injury, sedation, and optimizing residency training.

April also deserves recognition and congratulations for becoming a Fellow of the American College of Critical Care at the 2014 Annual Congress. In another wonderful honor, she and her husband Randal will be celebrating their two-year anniversary. They enjoy kayaking, fishing and tennis.

Please join me in recognizing Dr. April Quidley for her accomplishments and contributions to the profession.

**Miscellaneous**

**Frequently Asked Questions**

Where do I find an example of a poster presented at the SCCM Critical Care Congress?

Go to the SCCM website ([www.sccm.org](http://www.sccm.org)) and log into "My SCCM." On the right-hand side of the screen, click on Clinical Pharmacology and Pharmacy Section. Under Links, click on 2014 CPP SCCM Congress Posters. Several of the posters presented by members of the section can be found here and are excellent examples.

**The Critical Care Pharmacotherapy Trials Network (CCPTN)**

The CCPTN soon will be sending invitation emails to past study site investigators regarding the initiation of two new projects:

- The study, “Current Practices and Safety of Medication Use During Rapid Sequence Intubation”
- A two-phase study evaluating delirium practices in critically ill patients
For interest in either project, please contact Prasad Abraham at pabraham@gmh.edu.

A call for new study proposal submissions will be sent in October. The announcement will be made via email to previous site investigators.

If you have an interest in participating as a study site in the future, please contact Prasad Abraham at pabraham@gmh.edu.

**Research Subcommittee Email Consult Service!**

*Trying to get a new research idea ironed out for IRB proposal? Have you hit an unexpected roadblock in data collection or analysis and want a second opinion?*

Reach out to the **NEW** SCCM CPP Research Subcommittee Email Consult Service for guidance from critical care peers from around the country! We welcome **any** and **all** questions or clarification points you may have regarding any point of the research process! The goal of this service is to provide effective, concise advice within one week or less. Contact the service at [CPPResearchConsult@gmail.com](mailto:CPPResearchConsult@gmail.com).

We will be building a compendium of research-focused literature published over the years and uploading these as references in the iRoom! Please be sure to check this out as we are adding new papers regularly from research series in journals such as the *Journal of the American Medical Association*, *Chest*, *Circulation*, and *Lancet*! We look forward to hearing from you soon!

Communications Committee members are charged with publishing the newsletter. Thanks to the following members:

Deepali Dixit (Chair)  
Simon Lam (Chair-Elect)  
Amy L. Dzierba (Member at Large)  
Kate Adamczyk  
Farooq Bandali  
Kim Berger  
Aida "Rebecca" Bickley  
Marilyn Bulloch  
Darlene Chaykosky  
Chris Droge  
Michaelia Dunn  
Diana Esaias  
Stacey Folse  
Amanda Giancarelli  
Daryl Glick  
Payal K. Gurnani  
Susan Hamblin  
John Hammer  
Angela Haskell  
Tudy Hodgman  
Julie Kalabalik

Kirstin Kooda  
Jim Landzinski  
Xi Liu-Deryke  
Jason Makii  
Tom Moran  
Justin Muir  
Aljuhani Ohoud  
Mona K. Patel  
Tom Smooth  
Angela Haskell  
Tudy Hodgman  
Julie Kalabalik  
Joanna Stollings  
Ed Sypniewski  
Calvin Tucker
Featured CPP Resources

- Are you stuck on a research-related question? Consider reaching out to the experts in the CPP Research Committee by emailing cppresearchconsult@gmail.com.

- Do you have a manuscript or grant that you would like reviewed by a content expert? If so, consider emailing the Research Committee Chair at Frazee.Erin@mayo.edu.

Upcoming SCCM Congress Meetings – Save the Date!

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