Missouri Society of Health-System Pharmacists Newsletter November/December 2016

Season's Greetings from MSHP

Laura Butkievich, MSHP President

The holiday season is upon us! It is a busy time of year both in our personal and professional lives. MSHP has also been busy with activity. Each committee within MSHP has been working hard on accomplishing their objectives from the MSHP strategic plan.

- The Membership Committee is busy updating our membership database and working on a new member packet.
- The Newsletter Committee has just picked new theme topics for the newsletter for the upcoming 2017 calendar year.
- The Programming Committee has been busy planning the Spring meeting to occur March 31 – April 1, 2017 in Collinsville, Illinois (in conjunction with the Illinois Council of Health-System Pharmacists).
- The Public Policy Committee has been working to develop advocacy plans for technician roles in health-system pharmacy, pharmacist prescribing, and how to support a prescription drug monitoring program in Missouri.
- The Website Committee is looking to start redesigning the MSHP website.

If you are looking for a way to get more involved in MSHP, please consider joining one of the MSHP Committees. Contact MSHP for more details on how to get involved at mshp@qabs.com. Looking to get more formally involved in MSHP in the coming New Year? MSHP has several committee Vice Chair positions open. These individuals will serve as Vice Chairs until June 2017 and then move into a one year Chair appointment starting in July 2017. We are looking for Vice Chairs for the following MSHP Committees: Newsletter, Public Policy, and Website. If you are interested in one of these positions, please email Laura Butkievich at butkievichl@health.missouri.edu.

Recently Sarah, Jeremy, and I attended the Presidential Officer's Retreat in Chicago, Illinois sponsored by ASHP. At this retreat, we were able to meet with leaders from other state health-system pharmacy organizations and to share best practices to use within our organizations. At the retreat, we also listened to the keynote speaker, Gabrel Eckert, who is the author of the book "From Insight to Action: 6 New Ways to Think, Lead and Achieve." The retreat provided a lot of ideas that we now want to put into action for MSHP! We will be bringing these ideas forward to the MSHP Board of Directors and the MSHP membership in the coming year.

Happy Holidays from MSHP!

December/January MSHP Member Checklist:

- ☐ Save the date for the MSHP & ICHP Annual Conference: *March 31-April 1 2017* at The Gateway Center
- ☐ Save the date for abstract submissions for the Annual Conference: *January 30th*
- ☐ Contact MSHP for more details on how to get involved in a committee at mshp@qabs.com
- ☐ MSHP January/February Newsletter Deadline: *January 9th*. Topic: Psychiatry
- ☐ Nominate a MSHP member for one of the R&E Awards. Deadline: *February 1st*

Regulatory Update

Bert McClarey, RPh

Medication Therapy Services: Practicing at the Top

The Board of Pharmacy (BOP) emphasized during strategic planning discussions this year that the profession is responsible for practice advancement and the Board is responsible for protecting the public. It has been almost ten years since the medication therapy services (MTS) legislation was passed in 2007. What's next in MTS practice in Missouri? Are you practicing at the top of your license? Should we be talking about the next step?

The BOP must promulgate any required rules to implement practice changes, based on legislation. In 2009, subsequent to the 2007 statutory allowance for MTS, I circulated a draft rule to generate interest in rulemaking. The rule was required to implement MTS protocol practices. The BOP appointed a diverse Working Group to draft language for a rule, eventually becoming effective in 2012. The BOP Hospital Advisory Group will soon be discussing the current rule language in relation to current hospital/health system practice.

ASHP and MSHP promote Practice Advancement Initiatives (PAI). Such initiatives encourage the profession to move practice towards a higher standard. The ASHP PAI, the successor to the Pharmacy Practice Management Initiative (PPMI) of 2010, promotes "futuristic practice models that support the most effective use of pharmacists as direct patient care providers, and provides guidance related to quality of care and cost efficiency issues." Most of these activities can be achieved effectively with little additional regulatory oversight. The only exception is for activities provided through traditional practice acts and facility licensing standards.

State practice acts allow a form of physician/pharmacist agreements, generally known as collaborative practice. In Missouri, this is known as providing MTS by physician/pharmacist protocol. Many states, including Missouri, allow the pharmacist semi-independent authority to initiate or modify medication therapy. Nine states allow an advanced practice concept that includes semi-independent prescribing of controlled substances. States may use formal titles such as Pharmacist Clinician, Clinical Pharmacist Practitioner or Advanced Practice Pharmacist. Advanced practice credentialing, certification requirements, and permissible clinical activities vary widely from state to state.

In Missouri Section 338.010 RSMo states that pharmacists shall not "… diagnose or *independently* prescribe pharmaceuticals" (emphasis added). It provides authority for pharmacists to engage in written protocols for medication therapeutic plans. The law also requires the BOP and Board of Healing Arts to jointly promulgate rules for MTS. The rules that were promulgated allow pharmacists to "modify medication therapy," a term that was coined specifically for the MTS rules. The physician/pharmacist protocol process is more properly called "interdependent prescribing." However, that term was not defined and use of the term "prescribe" was avoided completely in the rules.

The MTS protocol rule states that when a pharmacist modifies medication therapy and a medication is to be dispensed, "… the pharmacist shall create a prescription … under the authorizing physician's name." A pharmacist is not allowed to sign a written or electronic prescription with the pharmacist's name or the physician's name. A telephone prescription must be "created" by the pharmacist, as an agent of the physician. This process can be burdensome and violates patient safety standards discouraging oral prescriptions. However, it meets the provisions outlined by the rule.
The rule does not allow a pharmacist to modify controlled substances medications. Since there is no pharmacist controlled substances authority provided in

the MTS statute, the rule states that "A pharmacist may be authorized by protocol to modify a patient's *non-controlled substance* medication therapy" (emphasis added). Both prescribing and controlled substances authority are specifically allowed by statute for advanced practice registered nurses (APRNs), physician assistants (PAs) and assistant physicians (APs).

Pharmacists, APRNs, and PAs are usually described by federal agencies as mid-level practitioners. The DEA will issue mid-level practitioner registrations only to individuals who have both prescribing authority and controlled substances authority granted by the state. The DEA recognizes in its mid-level practitioner descriptions that APRNs, PAs and APs in Missouri are given limited authority through collaborative practice.

Missouri controlled substances law requires registration with BNDD, a DHSS agency. Section 195.070 RSMo names prescribing practitioners with authority to prescribe controlled substances by specific title, including APRNs, PAs and APs. No reference is made to pharmacists.

When pharmacists are ready to ask for prescribing and controlled substances authority, there will be likely opposition from physician groups, especially from the Missouri Association of Osteopathic Physicians and Surgeons. These organizations traditionally oppose any incursion into medical practice by other professionals. In 2007 the Missouri State Medical Association conceded that, after several years of legislative efforts by pharmacists, it was time to legally recognize MTS by protocol. The legislation benefitted greatly from a federal reimbursement mandate that immunization by pharmacists be specifically allowed in state law.

It would be to the profession's benefit to develop a collaborative proposal with pharmacy organizations and other interested groups. At the appropriate time, such a proposal can be introduced to the legislature. APRNs, PAs and APs, who are allowed to diagnose and prescribe, are required to have advanced education and training. Their prescriptive authority is limited by statute to certain controlled-substance schedules and quantities. Physician groups will likely demand advanced credentials and restrictions on schedules, quantities or practice settings for pharmacists. A proposal should include clear evidence of the success of current MTS practices in Missouri and the success of advanced clinical practices, including prescribing, in other states.

I have discussed this briefly with individuals and groups and received mixed responses. Some persons simply accept the limitations. Others, such as those involved with pain management, believe that definitive prescribing and controlled substances authority should be allowed.

Advanced practice was briefly mentioned during the last BOP meeting, including the caution regarding physician opposition. Pharmacist prescribing appeared on the last MSHP Public Policy Committee agenda. MSHP has a PAI Task Force that will be a lead participant in this effort. MPA established the Missouri Pharmacist Care Network several years ago. The Department of Social Services MoHealthNet (Medicaid) reimburses pharmacists for certain MTM services. Federal provider status legislation is co-sponsored by almost 350 members of Congress, including 10 of 16 from Missouri. The Mo Pharmacy Coalition is no longer active. I am not familiar with activities of MoACCP, MoASCP or the pharmacy schools, but they or others may be discussing this issue.

PAI encourages pharmacists to "practice at the top of your license." In Missouri, practicing at the top of your license is not enough; your license should allow you to practice at the top of your competence. Are these restrictions merely an inconvenience or do they inhibit your best patient care? Should the MTS statute be re-visited? Are you ready to take the next step?

Board of Pharmacy Update

- The Board of Pharmacy is required to review all current rules for appropriateness over the next two years. The first rules reviewed at the October 26

meeting included Administration by Medical Prescription Order, Administration of Vaccines by Protocol and Non-dispensing Activities. A schedule of review is published on the Board's website and public comments are encouraged. Rules to be reviewed at the January meeting include Pharmacy Technician Registration and Automated Dispensing and Storage Systems.

- The Strategic Plan report is not yet available. The Board will select priority recommendations and develop action steps.
- The proposed rule allowing pharmacies to accept non-controlled substances for return has been filed and will probably be effective in early 2017.
- Representatives to a NABP meeting heard comments that other states are gravely concerned about hospital rule enforcement by surveyors from TJC and CMS. They cannot depend on the surveyors to detect problems, including diversion and sterile compounding. They encourage state monitoring.
- BOP staff members Katie DeBold and Tom Glenski presented a program on sterile compounding to DHSS surveyors to assist them in evaluating sterile compounding services in hospitals for DHSS licensing and CMS certification surveys.
- The Class B Hospital Pharmacy Guidance document was reviewed for the first time by the Board, and suggested language revisions will be reviewed by the Board and the Hospital Advisory Committee.

BOP Hospital Advisory Committee

The Class B Hospital Pharmacy Guidance document has been the priority topic for several meetings. The current draft is a 15 page document that provides compliance information for Class B licensed pharmacies. Topics discussed include:

- An overview of the Class B Hospital Pharmacy license
- License requirements
- Licensure in "DHSS licensed premises"
- Non-dispensing activities not requiring a Class B license
- Scope of Class B activities
- Dispensing by prescription or medication order
- Drug distribution to hospital/health system entities
- Labeling requirements
- Sterile compounding
- Technician activities
- Medication therapy services
- Immunization and administration of medications
- Class J shared services
- Record-keeping

This Guidance applies *only* to activities in areas included *under BOP jurisdiction of a Class B license*, such as those related to dispensing based on a prescription, dispensing based on a medical order that is to be administered to a patient onsite, MTS conducted as part of the Class B license and distribution from the Class B pharmacy to other entities.

The document does *not* include guidance for activities that *do not fall under the Class B license*, such as MTS, administration or distribution that occurs from areas not included in the Class B license. A separate guidance document will be developed that will discuss the relationships between BOP, DHSS and other health system entities for non-Class B activities, or for any activities in a hospital or health system entity that are under BOP jurisdiction when the hospital or other entity does not maintain a Class B license.

The HAC recommends that a separate "hospital pharmacy" rule be developed to include special requirements or allowances for hospital/health system practices, similar to the purpose of the long term care rule. The initial draft will include primarily Class B topics, such as distribution, dispensing and labeling requirements. Other topics will be discussed later and considered for special rulemaking, such as MTS protocols, records and notifications. The special section from the Administration by Medical Prescription Order rule will be recommended for inclusion.

One rule topic that has had multiple discussions is the potential for a Class B pharmacy to provide stock medications outside of the Class B license area in a clinic

or facility that is not included in the hospital licensed premises. Physician clinics and similar direct care facilities, such as urgent care or imaging centers, are not licensed in Missouri. Neither DHSS nor BOP have jurisdiction over medications in these facilities, even when they are hospital owned. Patient care and medications are under the control of a physician, and the HAC believes medication distribution and control would be safer and more efficient with complete pharmacy responsibility. Physicians generally agree, especially for controlled substances. The HAC is considering revisions to current rule language for automated dispensing systems and/or physician clinic pharmacy licenses.

The MTS rule will be reviewed at the next meeting. The original rule that was effective in 2012 was drafted with hospital participation and an allowance was included for physician notification, but there may be other areas of protocol requirements and records that are redundant or inappropriate for hospitals. The interface between "inpatient" and "outpatient" services also requires clarification when MTS are provided from a clinic or facility that is included in the hospital licensed premises, but a prescription will be filled for use by the patient outside of the hospital.

Joint rulemaking authority by BOP and DHSS is one of the provisions authorized by SB 808 in 2014. The agencies have authority to jointly promulgate rules governing medication distribution and provision of medication therapy services. There is no requirement for joint rulemaking, and DHSS may independently promulgate rules relating to pharmacy services and medication management under its licensing authority. Since proposed changes to DHSS rules have been reviewed and approved by BOP, there is no urgency to determine which subjects should be addressed with joint rules. This process will be addressed later.

BOP Pharmacy Technician Working Group Topics

The BOP Technician Working Group met in August and September, initially recommending three categories: Registered Support Staff, Registered Technician and Advanced Practice Technician. There was majority support for considering advanced roles, and less opposition than in the last technician working group five years ago.

An extensive list of specific activities was reviewed for each category. The Advanced Practice Technician category tentatively includes sterile compounding, nuclear, tech-check-tech, remote supervision and a variety of clinical support activities.

Specific recommendations for Advanced Practice Technician will be discussed at the next meeting.

THANK YOU!

A big thanks to UMKC and STLCOP for sponsoring the Missouri Reception at ASHP Midyear Clinical Meeting!

Affiliate Chapter News and Events

Mid-Missouri Society of Health-System Pharmacists (MMSHP)

Upcoming Events:

January 12th: Sponsored Program

March 9th: Sponsored Program

April: Sponsored Program, date TBD

May/June: pharmacy resident CE programs

President: Jordan Anderson, PharmD, BCPS, BCPPS (AndersonJord@health.missouri.edu)

Saint Louis Society of Health-System Pharmacists (STLSHP)

Upcoming Events:

January 23rd: Preceptor Development hosted with STLCOP

President: Mike Daly, PharmD, MSCI, BCPS (Michael.Daly@ssmsluh.com)

Greater Kansas City Society of Health-System Pharmacists (GKCSHP)

Upcoming Events:

January 16th: Annual Membership Drive @ Nick and Jake's- 6:00pm. Announcement of 2016 Awards and Installation of 2017 Board Members

January 2017 (Dates TBD): members of GKC will be teaming up with the UMKC Student Society of Health-System Pharmacists (SSHP) to volunteer at the Ronald McDonald House

Mark your Calendar for ***February 16th, March 16th, April 20th, May 18th*****:** Location and Topics TBA

Don't forget about 2017 GKCSHP meetings starting in February. All meetings will be scheduled the third Thursday of every month. Stay Tuned for topics for the presentations.

Member Spotlight:

Congratulations to Katie Korte on her publication in American Journal of Health-System Pharmacy, Pharmacists' guide to the management of organ donors after brain death

Board Certifications: Erin Pender (BCCCP), Katie Korte (BCCCP), Alex Oschman (BCPPS), Mike Axelsen (BCPS), Michael Moody (BCPS), Jake Sumner (BCPS).

President: Erin Pender, PharmD, BCPS, BCCCP (erin.pender@tmcmed.org)

Missouri Society of
Health-System Pharmacists Newsletter
November/December 2016

MSHP Member Spotlight

Meet your Current MSHP Treasurer

Megan Musselman, PharmD, BCPS

Megan Musselman is an Emergency Medicine/Critical Care Clinical Pharmacy Specialists at North Kansas City Hospital. She attended pharmacy school at Creighton University. Megan completed a PGY-1 Pharmacy Practice Residency at University of Illinois at Chicago and subsequently completed an Emergency Medicine PGY-2 at Detroit Receiving Hospital. She also has her Masters in Clinical Toxicology from University of Florida. In her position at North Kansas City Hospital she loves that she has the ability to work closely with physicians in the emergency department and ICU. She has a lot of autonomy and she gets to be a very active team member during acute situations. She is currently the MSHP treasurer and a member for the GKCSHP affiliate chapter. She also is very active in other professional organizations and serves as the ACCP Emergency Medicine PRN Chair, ASHP Section Advisory Group Emergency Medicine Member, and is a member on the ACCP CCSAP Critical Care Standards Committee. In her spare time, her hobbies include gardening and sewing.

Know a member who you think should be featured in the next membership spotlight? Contact the newsletter committee for more information!

MSHP R&E Foundation

R&E Call for Award Nominations

Davina Dell-Steinbeck, PharmD, BCPS

MSHP Research and Education Foundation Board Member

MSHP R&E Foundation is currently accepting submissions and nominees for several awards. The deadline for all submissions and nominations will be February 1st, 2017.

MSHP R&E Best Practice Award in a pharmacy directed initiative. The theme for the 2017 award focuses on **Medication Management in Care Transitions.**

Applicants will be judged on their descriptions of programs and practices currently employed in their health system. The following criteria will be utilized:

- Inventiveness of the program
- Significance of the program to the health system
- Demonstration of benefit to patient care as supported by program evaluation data
- Significance of the program to pharmacy practice
- Quality of submitted program report
- Relevance to other institutions

Applicants must be active MSHP members practicing in a health-system setting such as a large or small hospital, home health, ambulatory clinic or other health care system. More than one successful program from a health system may be submitted for consideration.

Award recipient will receive half off their meeting registration, a plaque and a $250 honorarium.

Submission Instructions: A program summary not to exceed 400 words must be submitted with the application and include the following information.

- Background – description of need for program
- Goals and specific aims of the program
- Program description/methods – description of development process, role(s) of the pharmacist, timeline
- Results - when results are not yet available, include a description of how impact of the program will be measured
- Conclusion – established and/or expected clinical impact of the program
- Submissions may also include any pictures, graphs, figures or data tables that support the summary. Each of these must be clearly labeled and described. Such information will not count against the 400 word limit.

A poster of the program will be highlighted during the Spring Meeting Poster Session. The award recipient will be honored at a fundraising event during the Spring Meeting and have the opportunity to provide a brief podium presentation detailing the implementation and impact of the project to the attendees.

Email your submission to mshp@qabs.com with Best Practice Award Submission in the subject line.

MSHP R&E Best Residency Project Award

The Best Residency Project Award recognizes innovation and outstanding performance in a pharmacy residency project. A poster of the program will be highlighted during the Spring Meeting Poster Session.

Applicants will be judged based on the following criteria:

- Inventiveness of the project
- Significance of the project to the health system
- Demonstration of benefit to patient care as supported by project evaluation data
- Significance of the project to pharmacy practice
- Quality of submitted project report
- Relevance to other institutions

Applicants must be active MSHP members completing a residency in a health-system setting such as a large or small hospital, home health, ambulatory clinic or other health care system.

Award recipient will receive half off their meeting registration, a plaque and a $250 honorarium.

Submission Instructions**:** A program summary, not to exceed 400 words, must be submitted with the application and include the following information.

- Background – description of need for project
- Goals and specific aims of the project
- Results - when results are not yet available, include a description of how impact of the project will be measured
- Conclusion – established and/or expected clinical impact of the project

Email your submission to mshp@qabs.com with Best Residency Project Award Submission in the subject line.

Garrison Award

The Garrison award was established in 1985, named after Thomas Garrison for his long standing support of MSHP (past-president 1974-1976), ASHP (past-president 1984) and numerous professional and academic contributions to Pharmacy. The Garrison Award is presented each year to recognize a candidate with sustained contributions in multiple areas:

- Outstanding accomplishment in practice in health-system pharmacy
- Outstanding poster or spoken presentation at a state or national meeting
- Publication in a nationally recognized pharmacy or medical journal
- Demonstrated activity with pharmacy students from St. Louis or the UMKC Schools of Pharmacy
- Development of an innovative service in a health-system pharmacy in either education, administration, clinical service, or distribution
- Contributions to the profession through service to ASHP, MSHP and/or local affiliates

Each letter of nomination must include:

- Name, work address, and telephone number of nominee
- Name, work address, and telephone number of nominator
- Sufficient explanation and documentation of the nominee's accomplishment(s) to allow a proper decision by the selection committee
- Curriculum Vitae of the Nominee

To be considered for the Garrison Award, **the nominee must be a current, active member of the Missouri Society of Health-System Pharmacists**. The winner will be selected by the Board of Directors of the MSHP Research and Education Foundation.

Email your nomination to mshp@qabs.com with Garrison Award Submission in the subject line.

Preceptor of the Year Award

MSHP R&E Foundation is pleased to honor a health system pharmacist for outstanding service to the profession as a preceptor to pharmacy students and/or residents. Below are the Criteria and Procedures to nominate a preceptor for the award.

Eligibility:

- Must be a member of MSHP;
- Must have been a clinical preceptor for minimum of 3 years;
- Must have not received the award within the last five years; attention will be given to previous nominations.

Criteria:

The award will be presented to a health system pharmacist that exemplifies the **core values** (Professionalism, Desire to educate and share knowledge with students, Willingness to mentor, Willingness to commit the time necessary for precepting, Respect for others, Willingness to work with a diverse student population) and the following characteristics:

- Partner in education: Is actively involved in instructing and educating in pharmacy practice
- Role model: Demonstrates willingness to mentor and serve as an example
- Experience: Has depth of experience and knowledge in area of expertise
- Coaching: Provides timely and meaningful feedback to the learner
- Enthusiasm: Demonstrates passion towards the profession and advancement of practice
- Professionalism: Conducts himself/herself with highest level of dignity and professionalism
- Teamwork: Facilitates team work and approach to patient care
- Opportunity: Creates innovative learning experiences and opportunities to for growth
- Research: Makes regular contributions to the profession through papers or presentations
- Education

- Evaluation
- Investment
- Negotiation
- Guidance

Support for Nomination: Please briefly explain (max 500 words) the ways in which the nominee models these core values. Email your submission to mshp@qabs.com with Preceptor of the Year Award Submission in the subject line.

SAVE THE DATE!
MSHP & ICHP 2017
Annual Conference
When: March 31st – April 1st 2017
Where: The Gateway Center
Poster Abstract deadline: January 10th

Featured Articles

Review of patiromer: a novel treatment for chronic hyperkalemia

Lisa Boone, PharmD Candidate 2017
Stephen Schafers, PharmD, BCPS

Patients with chronic kidney disease (CKD) are predisposed to hyperkalemia. CKD patients with concomitant comorbidities, such as diabetes and/or heart failure, have a high risk of developing hyperkalemia.[1-4] Current diabetes and heart failure guidelines recommend use of renin-angiotensin-aldosterone system (RAAS) inhibitors for their morbidity and mortality benefits in select patients.[5-7] Unfortunately, the CKD patient population with diabetes and/or heart failure may not receive these first-line therapies due to existing hyperkalemia at baseline, or subsequent hyperkalemia once RAAS inhibitor therapy is initiated. Furthermore, other medications including herbal medications, beta blockers, digoxin, non-steroidal anti-inflammatory drugs, azole antifungals, heparin, and trimethoprim-sulfamethoxazole may also increase serum potassium levels.[1]

Potassium balance is regulated by homeostatic mechanisms, primarily in the kidneys (90%), but also via the colon (10%).[3] Factors that may influence potassium homeostasis include secretion rate, total potassium stores, and dietary intake.[1, 2, 8] Potassium excretion is driven by sodium absorption in the renal tubules and collecting ducts. Sodium is reabsorbed through epithelial sodium channels (ENaC), and the lumen becomes more negatively charged. Potassium is then excreted into the lumen to counter the negative charge. In healthy individuals, increased potassium levels stimulate the release of aldosterone. Aldosterone increases the sodium influx via ENaC and facilitates an increase in potassium excretion.[1,3,8] Studies suggest that aldosterone is the driving factor that influences potassium regulation, rather than glomerular filtration rates or tubule function.[1,8] Patients using angiotensin converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARBs), or mineralocorticoid receptor antagonists (e.g. spironolactone) have impaired aldosterone secretion and consequently impaired potassium regulation. Additionally, CKD and heart failure patients are often placed on sodium restricted diets. Sodium is required for adequate renal potassium secretion and excretion. Therefore, potassium excretion is gradually shifted towards the gastrointestinal pathway. The distal colon contains the highest level of potassium, making its location an ideal target for potassium binders, especially in CKD patients.

Current approaches to manage chronic hyperkalemia include dietary restrictions, discontinuing RAAS inhibitors, initiating diuretics, or utilizing potassium-binding medications.[1-4] The use of sodium polystyrene

sulfonate (SPS) is limited by poor tolerability, potential for sodium overload, and the risk for gastrointestinal necrosis. The lack of tolerability warrants the development and investigation of new potassium-binding agents, such as patiromer.

Patiromer (Veltassa®), a new potassium-binding agent, was recently introduced in the market as a safe, well-tolerated, and predictable treatment for chronic hyperkalemia. Patiromer is formulated into small, emulsified spheres that form a suspension.[9] The active moiety contains a fluorine-substituted carboxylic acid, yielding a high electron withdrawing effect. Upon administration, it remains inactive until it reaches the colon where it is activated by the physiological pH in the colon, utilizing calcium as the exchange ion. Patiromer has a low molecular weight, allowing for an increased binding capacity at a pH of 6.5 to 12.0 in vitro.[2,9] The formulation contains five to fifteen-fold less sorbitol than SPS, and no osmotic diuresis has been observed.[2] Studies report no significant changes in calcium levels and hypercalcemia has not been reported.[2,9-12] Patiromer is contraindicated for acute hyperkalemia and should be avoided in patients with severe constipation, bowel obstruction, or bowel impaction. Patiromer is generally well-tolerated, with common adverse effects including constipation, diarrhea, and hypomagnesemia. Studies found that less than 3% of patients discontinued the medication due to gastrointestinal intolerance, which decreased with continued therapy.[8-12] No patients experienced magnesium levels < 1.0 mg/dL, and arrhythmias secondary to hypomagnesemia were not reported.[9-12] No severe adverse events were reported in clinical trials.[9-12]

Three main clinical trials have evaluated patiromer: PEARL-HF, AMETHYST-DN, and OPAL-HK.[10-13] PEARL-HF was conducted in patients with chronic heart failure and a history of hyperkalemia. Patients were randomized to patiromer 30 grams per day or placebo with subsequent initiation of spironolactone 25 mg per day. Patients receiving patiromer had a difference in serum potassium levels of -0.45 mEq/L compared to placebo at 28 days ($p < 0.001$). There was also a statistically significant lower incidence of hyperkalemia ($K^+ > 5.5$ mEq/L) in the patiromer group (7.3%) compared to the placebo group (24.5%). In patients with CKD, the potassium lowering effects were more prominent with a difference of -0.52 mEq/L ($p = 0.031$). More patients receiving patiromer tolerated a higher 50 mg/day dose of spironolactone (91% vs 74%, $p = 0.019$). The PEARL-HF study demonstrated that potassium reduction was greater in patients with higher baseline serum values. In patients with severe hyperkalemia ($K^+ > 6.0$ mEq/L), serum potassium levels were reduced to 5.5 mEq/L, but the same dose demonstrated less effect in patients with decreased potassium baseline values.

The AMETHYST-DN was a Phase II study of patients with Type II diabetes and CKD. The primary objective was to identify an appropriate patiromer dose.[10] This study involved an evaluation period to identify hyperkalemia in patients on home RAAS inhibitor therapy or patients receiving study-initiated losartan. Both groups could receive spironolactone for additional blood pressure control. Patients with pre-existing hyperkalemia or hyperkalemia during the evaluation period were eligible for the treatment phase of the study. Patients were then stratified based on serum potassium levels and patients in each stratum were randomized to receive 8.4, 16.8, 25.2, or 33.6 grams per day. Patients receiving greater than 25.2 grams per day in each stratum did not benefit from increased potassium lowering effects irrespective of hyperkalemia severity. Therefore, the conclusive dose established was 8.4-25.2 grams per day.

The OPAL-HK trial evaluated patients with CKD who were receiving RAAS inhibitors with potassium levels of 5.1 to 6.5 mEq/L.[11] In mild hyperkalemia (serum potassium greater than 5.1 but less than 5.5 mEq/L), the mean titrated patiromer dose was 12.8 grams per day. The mean dose in moderate-severe hyperkalemia was 21.4 grams per day. The mean change in serum potassium levels from baseline to week 4 was -1.01 ± 0.03 mEq/L. (95% CI, -1.07 to -0.95). Seventy-six percent of patients attained a serum potassium level in the target range between 3.8 and 5.1 mEq/L, with a serum potassium level of approximately 4.5 mEq/L at the end of

treatment. Patients that attained a potassium level within the target range were included into a withdrawal phase, where patients were randomized to continue patiromer or receive placebo treatment. Within 4 weeks of the withdrawal phase, the mean change in potassium in the placebo group increased by 0.72 mEq/L while there was no change in mean serum potassium in the patiromer group. The OPAL-HF trial demonstrated that the CKD patient population with hyperkalemia could maintain RAAS inhibitor therapy with a reduction in serum potassium levels and a decrease recurrence of hyperkalemia.

Patiromer was FDA approved in October 2015 for the treatment of hyperkalemia. It is available in single dose packets of 8.4, 16.8, and 25.2 grams. It is recommended to start at the lowest dose and increase the dose at weekly intervals if necessary, with the maximum daily dose of 25.2 grams. It is recommended to take patiromer with food to minimize gastrointestinal discomfort. Patiromer has specific administration instructions. The patient should measure 1/3 cup of water, pour half this amount into a glass, then add the full contents of the patiromer packet, and stir. Finally, add the remaining half portion of water. It should be noted that patiromer is insoluble in water, and it will remain cloudy. After preparation, patiromer should be consumed immediately. Due to its high in vitro medication binding capacity, the manufacturer suggests administering medications 6 hours before or 6 hours after patiromer. However, in vivo drug interactions have not been performed.[9] Patiromer is approved for once daily administration which will decrease the potential impact with concomitant medication interactions, although it was studied as a twice daily dose regimen.

Patiromer offers CKD patients the benefit of RAAS inhibitor therapy with a lower risk of hyperkalemia. Patiromer demonstrates a low-risk safety profile and a modest ability to lower serum potassium levels, reducing the incidence of hyperkalemia. An important consideration is that patiromer should only be used for treatment of chronic, mild-moderate hyperkalemia based on its modest ability to lower serum potassium levels. Patiromer may allow initiation or up titration of RAAS inhibitor therapy in CKD patients previously unable to tolerate RAAS inhibitor therapy secondary to hyperkalemia.

References

1. Sarafidis PA, Georgianos PI, Bakris GL. Advances in treatment of hyperkalemia in chronic kidney disease. *Expert Opin. Pharmacother.* 2015;16(14):2205-2212.

2. Li L, Harrison SD, Cope MJ, et al. Mechanism of action and pharmacology of patiromer, a nonabsorbed cross-linked polymer that lowers serum potassium concentration in patients with hyperkalemia. *J Cardiovasc Pharmacol Ther.* 2016;21(5):456-465.

3. Bakris GL. Current and future potassium binders. *Nephrol News Issues.* 2016;30(4):S27-31.

4. Einhorn LM, Zhan M, Hsu VD, et al. The Frequency of hyperkalemia and its significance in chronic kidney disease. *Arch Intern Med.* 2009;169(12):1156-1162.

5. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. *Am J Kidney Dis*. 2012 Nov;60(5):850-86.

6. Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure. *J Am Coll Cardiol.* 2016: S1071-9164(16)30550-4.

7. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2013;3:S1-S150.

8. Gennari JF. Hyperkalemia: an adaptive response in chronic renal insufficiency. *Kidney Int.* 2002;62(1):1-9.

9. VELTASSA ® (patiromer) package insert. Redwood City, CA: Relypsa, Inc; 2016 June.

10. Bakris GL, Pitt B, Weir MR, et al. Effect of patiromer on serum potassium level in patients with hyperkalemia and diabetic kidney disease: the AMETHYST-DN randomized clinical trial. *JAMA.* 2015;314(2):151-161.

11. Weir MR, Bakris GL, Bushinsky DA, et al. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N Engl J Med.* 2015;372(3):211-221.

12. Pitt B, Anker SD, Bushinsky DA, et al. Evaluation of the efficacy and safety of RLY5016, a polymeric potassium binder, in a double-blind, placebo-controlled study in patients with

chronic heart failure (the PEARL-HF) trial. *Eur Heart J.* 2011;32(7):820-8.
13. Schaefer JA, Gales MA. Potassium-binding agents to facilitate renin-angiotensin-aldosterone system inhibitor therapy. *Ann Pharmacother.* 2016;50(6):502-509.

Sepsis-3: The End of a SIRS Era

Alaina Dekerland, PharmD Candidate 2017, Shannon Piche, PharmD, BCPS

Sepsis, a complex pathophysiologic syndrome resulting in an inappropriate host response to infection, confers a significant degree of morbidity and mortality to those affected. Thus, it is crucial for clinicians to understand current standards for diagnosing individuals with suspected sepsis.

A 1991 consensus conference first introduced the systemic inflammatory response syndrome (SIRS) criteria for diagnosing sepsis in the presence of infection. At that time, sepsis with concomitant end organ dysfunction was termed "severe sepsis," which could progress to sepsis-induced hypotension, or "septic shock."[1] These guidelines remained unchanged until a 2001 task force recommended additional parameters for diagnosing sepsis, such as coagulation abnormalities, renal dysfunction, etc. However, the guidelines did not specify the relationship between the presence of these characteristics and an increased severity of illness or mortality risk.[2]

SIRS Criteria: The Problem

The SIRS criteria have remained the primary method in diagnosing sepsis for more than two decades despite clear clinical controversy.[3] It is well recognized that the SIRS criteria are not specific to the presence of infection, but instead a result of general inflammatory stimuli. Churpek, et al. demonstrated up to 47% of patients in the hospital setting with no infection or sepsis diagnosis exhibited ≥2 SIRS criteria at some point during their hospitalization.[4] However, recent evidence is also concerning for a lack of sensitivity in sepsis recognition with SIRS criteria. Kaukonen, et. al reported one in eight patients admitted to the intensive care unit with infection and new organ dysfunction met <2 SIRS criteria. Additionally, no mortality difference was observed between SIRS positive versus negative individuals.[5] This lack of sensitivity and specificity in sepsis diagnosis, in conjunction with the lack of clinical outcome data supporting current severe sepsis and septic shock definitions, necessitate use of an alternative method. As a result, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine joined to form a coalition tasked with re-defining sepsis.

Sepsis-3 Task Force, Identified Issues[6]:

- No gold standard for diagnosing sepsis (i.e., laboratory test)
- Previous definitions were not founded on clinical outcomes, rather they were formed based upon expert opinion
- SIRS is an ***appropriate*** response to the presence of an infection
- Severe sepsis terminology redundant, often misused
- Different variables for sepsis, septic shock identification resulted in a lack of consistent mortality rates in published literature

Sepsis-3 Guideline Update: Notable Changes:[6]

- Elimination of SIRS criteria in sepsis diagnosis, addition of Sepsis-related Organ Failure Assessment (SOFA) scoring system
- Introduction of qSOFA score screening tool in non-ICU patients (Table 1)
- Removal of severe sepsis nomenclature

Table 1. Quick Sequential Organ Failure Assessment (qSOFA)[6]

Altered Mental Status	Systolic Blood Pressure <100 mmHg	Respiratory Rate ≥ 22 per minute

Sepsis "is life-threatening organ dysfunction caused by a dysregulated host response to infection"

Due to the limitations of SIRS criteria, Sepsis-3 recommends against SIRS as the sole diagnostic standard for sepsis. The task force introduced the SOFA score, a

tool used to assess laboratory data for markers of organ failure, due to its validated efficacy in predicting morbidity and mortality.[7-9] In sepsis, organ dysfunction can be identified as an acute change from baseline SOFA score ≥2 points, secondary to infection. In individuals with no preexisting organ dysfunction and no prior laboratory data for comparison, it is assumed that the baseline SOFA score is zero.

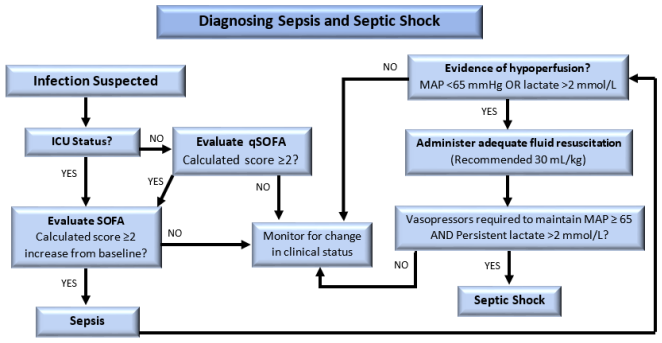
The task force also identified a new method, the qSOFA score, for screening (not diagnosing) individuals with suspected sepsis on general hospital floors or outpatient clinics. The qSOFA score evaluates three clinical parameters which are easily assessed at the bedside and do not require laboratory intervention. A qSOFA score ≥2 warrants further investigation (i.e., collecting data necessary to calculate the SOFA score) in order to definitively diagnose sepsis.[6]

Septic Shock "is a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone"

Shankar-Hari, et. al. performed a literature review comparing relative mortality rates based upon the presence or absence of certain clinical characteristics (hypotension, fluid or vasopressor requirements, and elevated serum lactate).[10] In this analysis, patients with both hypotension (mean arterial pressure [MAP] <65) and a serum lactate >2 mmol/L exhibited mortality rates in excess of 40%, versus 25% to 30% mortality reported in those without hypotension or an elevated lactate. Thus, the Sepsis-3 guideline reserves the diagnosis of septic shock to patients with hypotension requiring vasopressor therapy to maintain MAP ≥65 and a serum lactate of >2 mmol/L despite adequate fluid resuscitation.[6]

Sepsis-3, Controversies:

- SOFA scoring is complex, time-consuming, and may result in delay of patient care
- Diagnosis requires assessment of patient's baseline SOFA score, which is often unavailable
- Sepsis-3 criteria have not yet been recognized by the Centers for Medicare and Medicaid Services (CMS), making it difficult to implement the new guidelines into hospital protocols



References

1. Bone RC, Balk RA, Cera FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis. *CHEST*. 1992Jun;101(6):1644–55.

2. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med*. 2003Apr;31(4):1250–6.3.

3. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. *Crit Care Med*. 2013Feb;41(2):580–637.

4. Churpek MM, Zadravecz FJ, Winslow C, Howell MD, Edelson DP. Incidence and Prognostic Value of the Systemic Inflammatory Response Syndrome and Organ Dysfunctions in Ward Patients. *Am J Respir Crit Care Med*. 2015Oct15;192(8):958–64.

5. Kaukonen KM, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis. *N Engl J Med*. 2015Apr23;372(17):1629–38.

6. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016Feb23;315(8):801–10.

7. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016Feb23;315(8):762–74.
8. Vincent JL, Moreno R, Takala J, Willatts S, de Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med*. 1996Jul;22:707–10.
9. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter P, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. *Crit Care Med*. 1998Nov;26(11):1793–800.
10. Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016Feb23;315(8):775–87.

Upcoming Newsletter Topic for January/February Newsletter

Topic: Psychiatry

Submission Date: January 9th, 2017

Submit to Hannah Pope: Hannah.pope@bjc.org

Future Newsletter Topics & Deadlines:

March 13th
Specialty Pharmacy
May 8th
Pulmonary/Critical Care/Toxicology
July 10th
Pain Management
September 11th
Cardiology/Anticoagulation
November 13th
Infectious Diseases

Missouri Society of Health-System Pharmacists Newsletter November/December 2016

MSHP Board of Directors 2016-2017

President	Laura Butkievich	butkievichl@health.missouri.edu
President-Elect	Jeremy Hampton	hamptonjp@umkc.edu
Immediate Past President	Sarah Boyd	Sarah.Boyd2@Mercy.net
Secretary	Cassie Heffern	Cassie.Heffern@coxhealth.com
Treasurer	Megan Musselman	meganmusselman@gmail.com

MSHP Committee Chairs 2016-2017

Membership Committee	Alexandra Oschman	aoschman@cmh.edu
Public Policy Committee	Brian O'Neal	bconeal@cmh.edu
Newsletter Committee	Hannah Pope	Hannah.pope@bjc.org
Education and Programming	Abby Yancey	Abigail.yancey@stlcop.edu
Vendor Relations	Evanna Shopoff	eshopoff@pharmedium.com

Questions/Comments

If you have any questions or comments about MSHP Newsletter, please don't hesitate to contact the Newsletter Chair, Hannah Pope, hannah.pope@bjc.org or any other newsletter committee member.

2016-2017 MSHP Newsletter Committee Members

Hannah Pope, PharmD, BCPS

Anastasia Armbruster, PharmD, BCPS

Barb Kasper, PharmD, BCACP

Contact your fellow newsletter committee member for future 2017-2018 Membership Spotlights and Article Submissions!