



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

MSHP Membership Spotlight: Meet the President



**Jeremy Hampton,
PharmD, BCPS**

We would like to welcome Jeremy Hampton as our President of The Missouri Society of Health System Pharmacists! Dr. Hampton is a Clinical Associate Professor at UMKC School of Pharmacy, and Emergency Medicine Clinical Specialist at Truman Medical Center Emergency Department. Jeremy attended pharmacy school at UMKC School of Pharmacy. He then completed his Pharmacy Practice and Administration Residency at Duke University, with an emphasis in Emergency Medicine and Critical Care. Jeremy's affiliate is the Kansas City affiliate chapter of MSHP. Dr. Hampton has a very exciting position as a Clinical Associate Professor and Emergency Medicine Clinical Specialist, and describes what he loves about his job is that it is a "unicorn, it's one of those that you are convinced that doesn't really exist, but when you find it, you realize it's glorious." He has a job that no two days are the same, he may have his hands deep inside of a chest cavity on Monday and then Tuesday you may find him leading a committee or giving a lecture. He loves that he is able to practice pharmacy in a very hands-on manner, working in the trenches side by side with every other type of provider in the ED and he is actually responsible for making life or death treatment decisions. On the didactic front, he is able to shape the education not only of pharmacy students but also of medical students and residents. He would not trade this extremely fulfilling job for anything! Outside of work, his hobbies include aviation photography, flying airplanes, playing and coaching baseball, drawing, building stuff, and cooking. He once won an international photography competition that was judged by the one and only, John Travolta and sponsored by Breitling. The grand prize was a pilot license sponsored by Breitling and an awesome watch! Now that he has his pilot license, he would give any number of fingers and toes to have the chance to fly with the Blue Angels or Thunderbirds.

What is Jeremy most looking forward to while serving as President of MSHP?

"This is a very exciting time for the profession of pharmacy as we inch closer to being nationally recognized as providers. There are so many amazing minds and great pharmacy leaders within the state of Missouri and I'm looking very forward to working alongside of them as we advance our cause to show the nation what we can (and do) do as pharmacists!"

Thank you Dr. Hampton for being such an integral member of MSHP! We look forward to this year!

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



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

Regulatory Update

Bert McClary

May-June 2017

Board of Pharmacy Regulatory Update

Board of Pharmacy

The BOP met in open session on April 18 and 19.

- Several companies made presentations of automated dispensing systems, continuing the discussions begun at the February and March meetings. ADS types discussed included inpatient ADCs, remote tech monitoring by image, and outpatient direct patient access systems.
- Continuing the required rules review, several rules received comments and will be further reviewed for changes: sterile compounding, administration, LTCF, automated dispensing systems, MTS, standards of operation and Class J shared services.
- A LTCF rule sub-committee was recommended, and has since been appointed to meet June 16. The focus of the LTCF rule and the interest of the Board is the traditional system of providing prescriptions by retail pharmacies. However, some hospitals and health systems operate LTCFs and there is growing interest in alternate distribution systems. If you have an interest in health system LTCF issues, please contact Bert McClary (bertmcclary@gmail.com).
- The Technician Working Group report was discussed and a recommendation made to prepare a legislative proposal for next year, which may include language regarding remote supervision if the Board agrees to move forward with that topic. The current recommendation for technicians will be three categories, Registered Pharmacy Support Staff, Registered Pharmacy Technician and Registered Advanced Pharmacy Technician. Requirements for education and training will be included. Remote supervision was again discussed by the Board, with concerns expressed regarding standards of care. Future discussions will include additional data from other states and different models of supervision, including those specific to health systems.
- Five members of the public stayed to participate in a late afternoon strategic planning session, including three hospital pharmacists. Goals for the year include: Provide clear rules and regulations; expand strategic alliances with stakeholders, political entities, other Boards, and organizations; and increase communications to licensees

through videos, newsletter frequency and articles in other newsletters.

- An additional open session has been announced for June 23 to discuss proposed rule language and a legislative proposal. The next regularly scheduled meeting will be July 12.

BOP Hospital Advisory Committee

The HAC May 4 in Jefferson City.

- A BOP proposal would exempt the requirement for a Class J Shared Services license if the delivered prescription will be administered at the same site as the receiving pharmacy, potentially affecting prescriptions delivered for administration at remote hospital clinics.
- Administration by medical prescription order was discussed again. Draft proposals by HAC and BOP staff were merged to provide a final recommendation for BOP approval.
- Final Class B Guidance document language was approved for publishing.
- A new draft rule that will not be ADS specific will be developed to address distribution of medications to remote clinic locations. Current ADS rules (to be revised) for both prescription and non-prescription distribution concepts would supplement the general rule.
- There is concern that certain groups will oppose any BOP legislative effort that requires certification for advanced techs. Discussions of remote tech supervision for health systems will have to be clearly differentiated from current public discussions of “telepharmacy” remote supervision of techs in remote retail pharmacy locations.
- BOP LTCF rule discussion should include DHSS LTCF rules, ADS distribution from hospitals, on-site pharmacist medication control and distribution, in-house distribution systems, and transition of care from the hospital to the LTCF.
- No recommendations were made for changes to the MTS rule which will be discussed at the June BOP meeting, based on possible future MTS legislative changes that would require significant rule changes also.
- It was emphasized that attendance at BOP public sessions by hospital pharmacists is critical to provide information to the Board regarding rule and legislation issues. HAC members and the general public are strongly encouraged to participate.



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

- Individual HAC members have comments on the sterile compounding rule regarding technical issues, but will provide those directly to the Board without requesting HAC discussion.
- Neil Schmidt, who represents MSHP on the HAC, announced his resignation from the committee. MSHP will recommend a replacement to be appointed by the Board. Bert McClary requested that the committee select a new Chairperson in the near future. The HAC will meet next on July 17 and will review progress over the past 18 months and recommend future topics as well as meeting frequency and format.

2017 Legislation, Senate Bill 501

SB 501 sponsored by pharmacist Senator David Sater and handled in the House by pharmacist Representative Mike Stephens was passed. It is a final conference committee bill combining 14 health care subjects into one bill, including:

- Providing certain immunities from prosecution for assisting a person with a drug or alcohol emergency and authorizing a statewide standing order through DHSS for distributing an opioid antagonist.
- Providing for the prescribing, distribution and administering of epinephrine injectors by certain persons or groups outside of usual prescription requirements, and certain immunities from prosecution related to administration of epinephrine.
- Beginning July 1, 2018 compliance with Medicare conditions of participation shall be deemed to constitute compliance with the standards for hospital licensure. DHSS may enact additional requirements with statutory authority.
- Adds the phrase “by protocol” to the current requirement that a pharmacist shall administer vaccines (by protocol) in accordance with treatment guidelines established by the Centers for Disease Control and Prevention.
- Allows BOP to allocate funds in consultation with DHSS to develop a drug take-back program to collect and dispose of CII and CIII controlled substances.
- Changes to both physician assistant and assistant physician practice statutes were made, but language interpretations could not be confirmed by the Newsletter deadline.

“The scope of practice of a physician assistant shall
2 consist only of the following services and procedures:
3 (1) Taking patient histories;
4 (2) Performing physical examinations of a patient;

5 (3) Performing or assisting in the performance of routine
6 office laboratory and patient screening procedures;
7 (4) Performing routine therapeutic procedures;
8 (5) Recording diagnostic impressions and evaluating
9 situations calling for attention of a physician to institute
10 treatment procedures;
11 (6) Instructing and counseling patients regarding mental
12 and physical health using procedures reviewed and
13 approved by a
14 licensed physician;
15 (7) Assisting the supervising physician in institutional
16 settings, including reviewing of treatment plans, ordering
17 of
18 tests and diagnostic laboratory and radiological services,
19 and
20 ordering of therapies, using procedures reviewed and
21 approved by
22 a licensed physician;
23 (8) Assisting in surgery;
24 (9) Performing such other tasks not prohibited by law
25 under
26 the supervision of a licensed physician as the physician's
27 assistant has been trained and is proficient to perform;
28 and
29 (10) Physician assistants shall not perform or prescribe
30 abortions.
31 4. Physician assistants shall not prescribe [nor dispense]
32 any drug, medicine, device or therapy unless pursuant to a
33 physician supervision agreement in accordance with the
34 law, nor
35 prescribe lenses, prisms or contact lenses for the aid, relief
36 or
37
38 1 correction of vision or the measurement of visual power or
39 visual
40 2 efficiency of the human eye, nor administer or monitor
41 general or
42 3 regional block anesthesia during diagnostic tests, surgery or
43 4 obstetric procedures. Prescribing [and dispensing] of drugs,
44 5 medications, devices or therapies by a physician assistant
45 shall
46 6 be pursuant to a physician assistant supervision agreement
47 which
48 7 is specific to the clinical conditions treated by the
49 supervising
50 8 physician and the physician assistant shall be subject to the
51 9 following:
52 10 (1) A physician assistant shall only prescribe controlled



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

11 substances in accordance with section 334.747;
12 (2) The types of drugs, medications, devices or therapies
13 prescribed [or dispensed] by a physician assistant shall be
14 consistent with the scopes of practice of the physician
assistant
15 and the supervising physician;
16 (3) All prescriptions shall conform with state and federal
17 laws and regulations and shall include the name, address
and
18 telephone number of the physician assistant and the
supervising
19 physician;

20 (4) A physician assistant, or advanced practice registered
21 nurse as defined in section 335.016 may request, receive
and sign
22 for noncontrolled professional samples and may distribute
23 professional samples to patients; and
24 (5) A physician assistant shall not prescribe any drugs,
25 medicines, devices or therapies the supervising physician
is not
26 qualified or authorized to prescribe; and
27 (6) A physician assistant may only dispense starter doses
28 of medication to cover a period of time for seventy-two
hours or 32 1 less]. 2"

Affiliate Chapter News and Events

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

Upcoming Events:

July: No Meeting

August 17th: *Relypsa*, Location TBD

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

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

Upcoming Events:

July 29th: *Member Appreciation Event*, Sporting KC vs. Chicago Fire, Children's Mercy Park, 7:30 PM. More info on tickers and pricing coming soon!

[GKCSHP is now on Instagram! Follow us @gkcsHP!](#)

President: Bryan Schuessler, PharmD, M.S. (bschuessler@saint-lukes.org)

Saint Louis Society of Health-System Pharmacists (StLSHP)

Upcoming Events:

July: No Meeting

August 17th: *Repatha*, Location TBD

September 25th: StLSHP night at the ballpark honoring technicians and interns (Cardinals vs. Cubs)

President: Emily Owen, PharmD, BCPS, BCCCP



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

R & E Update

Congratulations to the 2017 R&E Award Recipients

Best Practice Award

Insulin Portfolio Consolidation in an Academic Medical Center
Michael A. (Tony) Huke, PharmD, BCPS
Clinical Manager-Medication Use Truman Medical Centers

Best Resident Project Award

Drug Usage Review of Nonionic Iodinated Contrast Media in Cardiac Catheterization Procedures
Jessica Brinkmeyer, PharmD
Resident, Southeast Hospital

Best Original Poster

Integration of Pharmacy Technicians into Decentralized Pediatric Pharmacy Services
Karrie Derenski, PharmD,
Cox Health

Second Place, Original Poster

Evaluation of Peripheral Opioid Antagonists Prescribed for Opioid Induced Constipation
Megan Nicklaus, PharmD
University of Missouri

Best Resident Poster

Evaluation of Parenteral Calcitonin in Hypercalcemia Treatment in a Community Hospital
Kari Righter, PharmD, Southeast Hospital

Second Place, Resident Poster

Safety and Efficacy of Enoxaparin Compared to Unfractionated Heparin for Venous Thromboembolism Prophylaxis
in Hemodialysis Patients
Melissa Green, PharmD
Missouri Baptist Medical Center

Best Student Poster

Medication Use Evaluation of Metformin in Patients with Chronic Kidney Disease
Miriam Belonwu, PharmD Candidate
UMKC School of Pharmacy at MU

Second Place, Student Poster

Aztreonam Medication Use Evaluation
Laken Brock, PharmD Candidate



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

Featured Articles: Critical Care “Two for the Price of One”

Sustained Neuromuscular Blockade in the Adult Critically Ill Patient

Jeremy Eutsler, 2017, PharmD Candidate
Jace Knutson, PharmD, BCPS, BCCCP

Neuromuscular blocking agents (NMBA) induce paralysis and are typically used to facilitate mechanical ventilation, tracheal intubation, and surgical procedures. While relatively uncommon in critically ill patients, there are clinical scenarios in which sustained blockade may be warranted. The society of Critical Care Medicine recently updated their guidelines for these instances. This article will review several of these recommendations as well as discuss general considerations and clinical pearls for NMBA utilization.

Indications for Sustained Blockade

Severe Acute Respiratory Distress Syndrome (ARDS)

The guidelines suggest a NMBA be administered by continuous infusion early in the course of ARDS for patients with a $P_{aO_2}/F_{iO_2} < 150$ (weak recommendation, moderate quality of evidence). Three multicenter randomized trials have evaluated the use of 48-hour cisatracurium infusions among adult patients with ARDS. All studies showed significant improvements in oxygenation in patients receiving NBMA compared with control groups. Additionally, reductions in the risk of death at 28 days and at hospital discharge were observed. No increase in the risk of ICU-acquired weakness was seen. Cisatracurium is the only agent formally studied in this setting.

Status Asthmaticus

Routine administration of an NMBA in mechanically ventilated patients with status asthmaticus is not supported (weak recommendation, very low quality of evidence). Three retrospective studies investigating patients who required mechanical ventilation for the management of acute asthma demonstrated an association between NMBA administration and ICU-

acquired weakness as well as longer duration of mechanical ventilation. If life-threatening situations such as severe hypoxemia, respiratory acidosis, or hemodynamic compromise that cannot be controlled by deep sedation, a NMBA trial is suggested (weak recommendation, very low quality of evidence).

Therapeutic Hypothermia Induced Shivering

Due to insufficient evidence, no recommendation is made for the routine use of NMBAs in patients undergoing therapeutic hypothermia following cardiac arrest. No trials have prospectively evaluated the outcomes of NMBA use in this setting. However, NMBAs may be used to manage overt shivering in therapeutic hypothermia (weak recommendation, very low quality of evidence). In theory, paralysis may be neuroprotective by assisting in achievement of target temperature more quickly and reducing oxygen consumption, but could also mask the presence of seizures.

General Care and Monitoring

Pain and Sedation

NMBAs possess no analgesic or sedating properties. Paralyzed patients without appropriate pain relief or sedation report feeling terrified and experiencing overwhelming pain. The guidelines recommend administering analgesic and sedative medications prior to initiation and throughout neuromuscular blockade with the goal of achieving deep sedation (good practice statement). If clinically appropriate, intermittent breaks from NMBA therapy may be useful for guiding agent titration utilizing validated assessment scales as this can be difficult to evaluate during paralysis.

Titration/Monitoring

Peripheral nerve stimulation with train of four (TOF) monitoring is commonly used to assess the degree of paralysis. While the guidelines suggest this method should not be used alone for monitoring and titrating neuromuscular blockade, it may be useful when used in conjunction with appropriate clinical assessment to



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

determine the depth of paralysis (weak recommendation, very low quality of evidence). In general, the lowest level of blockade that achieves clinical goal (ex. vent synchrony, cessation of shiver) should be targeted to minimize the adverse effects associated with sustained paralysis.

Eye Care

Scheduled eye care that includes lubricating drops or gel and eyelid closure should be a standard for patients receiving NMBA therapy (strong recommendation, low quality of evidence). Paralysis impairs ocular protective mechanisms and may lead to surface damage.

Glycemic management

Clinicians should target a blood glucose level of < 180mg/dL in patients receiving NMBAs (weak recommendation, low quality of evidence). Hyperglycemia appears to increase the risk of myopathy.

Dosing in Obesity

Clinicians should not use actual body weight and instead use a consistent weight (ideal or adjusted body weight) when calculating NMBA doses for obese patients (weak recommendation, low quality of evidence).

Agent Overview and Clinical Pearls

NMBAs are divided into depolarizing and non-depolarizing agents. Succinylcholine, the depolarizing agent, is generally only used to facilitate short procedures such as intubation. The non-depolarizing agents can be further divided into aminosteroids and benzyliisoquinoliniums.

Aminosteroids are all hepatically metabolized and renally excreted. Pancuronium is a long-acting agent and potential option for patients with normal hepatic and renal function. Clinical use may be limited by accumulation risks and cardiovascular side-effects. Vecuronium and rocuronium are intermediate-acting agents. Although no specific renal or hepatic dosing adjustments are recommended, accumulation would be an important consideration with prolonged usage and significant organ dysfunctions. This is especially true with

vecuronium, which possesses a more potent active metabolite.

Benzyliisoquinoliniums, including atracurium and cisatracurium, may be more preferable in patients with organ dysfunctions as they undergo Hoffman elimination and do not possess active metabolites. Degradation results in the metabolite laudanosine, a neurostimulant with possible toxic effects. While the clinical significance of this metabolite is thought to be minimal, it would be more likely to accumulate with atracurium use. Atracurium can also stimulate histamine release, while cisatracurium does not. Effects of release may be blunted by utilizing slower bolus doses or pre-medicating with an anti-histamine agent.

For a comparative table of NMBA agents, refer to Appendix A.

NMBAs possess many medication and disease state interactions, including but not limited to:

<i>Antagonized effects:</i> Hypercalcemia, phenytoin and carbamazepine, theophylline and caffeine, muscle trauma and large surface-area burns

<i>Potentiated effects:</i> Electrolyte imbalances (esp. hypermagnesemia), antibiotics (aminoglycosides, tetracyclines, clindamycin, vancomycin), certain cardiovascular agents, lithium, neuromuscular disorders, myasthenia gravis, hypothermia

While uncommonly used in this setting, it is noteworthy that reversal agents are available. *Refer to Appendix B for a comparative table.*

Conclusion

NMBAs are high-alert medications which may pose significant potential risks. Pharmacists have the ability to play a significant role in utilizing these agents as safely and effectively as possible by assisting with appropriate agent selection, screening for significant medication or disease state interactions, and promoting best practices related to supportive care and monitoring.



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

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Update on Neuromuscular Blocking Agent Use in Critically Ill Patients

Ivan Porto, Pharm.D. Candidate 2020
Paul Juang, Pharm.D., BCPS, BCCCP, FASHP, FCCM

Physiological and Pharmacological Overview of Neuromuscular Blocking Agents

Neuromuscular Blocking Agents (NMBAs) are a class of drug that engage in inhibitory action in the neuromuscular junctions of the body. There are two subclasses of NMBAs, depolarizing agents and non-depolarizing agents, which vary in indication, length of action, and adverse reactions. However, both classes achieve a similar goal: they prevent action potential

transmission in the neurons of muscle fascicles. This action leads to the induction of muscle paralysis, which can be useful for a variety of interventions in critically ill patients.

Depolarizing Agents

Depolarizing agents paralyze muscle fascicles by preventing neurons from being able to repolarize after firing an action potential.

Short length of action (10 minute maximum)	Fast induction of maximal blockade (30-60 seconds)
Narrow array of indications for use in the ICU due to short duration and long refractory period	Side effects (bradycardia, histamine release, potential for hyperkalemia)
Contraindicated in patients with hyperkalemia, myopathies, major burns, multiple traumas, extensive denervation of skeletal muscle and motor neuron injury	

Prominent Members	Mechanism of Action	ICU Indications
Succinylcholine	Continuous agonists to nicotinic receptors. Their binding allows an influx of ions. Ion-gated channels open and stay open, preventing the cell from returning to resting potential. Action potential cannot fire again, muscles become paralyzed.	Induction of paralysis for intubation

Non-Depolarizing Agents

Non-Depolarizing agents paralyze muscle fascicles by preventing action potential transmission via inhibition of neuromuscular transmitters from binding at target sites.

Medium-Long length of action (20-100 minutes)	Fast induction of maximal blockade, but slower than depolarizing agents (1-5 min maximum)
Wide array of indication	Side effects vary from agent to agent, but generally induce vagal blockade and histaminergic effect
Prolonged use can lead to ICU-acquired weakness	Must be used in combination with other sedatives/analgesics during neuromuscular blockade

Prominent Members	Mechanism of Action	Indication
Pancuronium Vecuronium Rocuronium Atracurium Cisatracurium	Competitive antagonists of nicotinic receptors. Prevent binding of acetylcholine at post-synaptic junction. Widespread neuromuscular blockade leads to fascicular paralysis due to inability of acetylcholine to reach their targets.	Induction of paralysis for intubation Prevention of shivering in patients on therapeutic hypothermia Facilitation of lung protection strategies in acute respiratory distress syndrome. Reduction of intracranial pressure in traumatic brain injuries

Updated Practice Guidelines

The most recent guideline expanded upon the previous two guidelines to include information on the indications and recommendations for use of NMBA's, more information on the nursing management of patients receiving NMBA's, on mechanical ventilation management for patients receiving NMBA's, on techniques and therapies to decrease complications and adverse effects related to the use of NMBA's, and on specific patient populations that may benefit from

NMBA's. The guideline divided the practice into "good practice guidelines" or "possible practice guidelines".

Good practice guidelines can be considered "good" because either the evidence supporting their use is strong, or because no possible alternative treatment exists beyond the use of NMBA's. However, even these good practice standards cannot yet be considered a standard of care without further evidence.

Possible practice suggestions lack the level of conclusively of those good practice guidelines; the study can only make weak recommendations or suggestions based on their findings. These suggestions could be implemented in institutions who do not currently have any protocols in place regarding the specific situation described.

Considerations and Monitoring

- Patients are typically monitored for pain via the use of a Behavioral Pain Scale (BPS) or the Critical Care Pain Observation Tool (CPOT) while level of sedation is monitored via the use of Richmond Agitation Sedation Score (RASS) or the Sedation Agitation Scale (SAS). Bispectral index (BIS) score monitoring can also be used to monitor the degree of sedation in a paralyzed patient.
- In patients on continuous paralysis, the goal TOF is 1-2 twitches/4 with the use of peripheral nerve stimulators.
- While the evidence is only anecdotal, one potentially important consideration is that practitioners verbally reassure patients who are being given NMBA's. Many patients who maintained awareness during neuromuscular blockade have stated that they remember being given positive emotional support. Even though the evidence of necessity for this consideration is inconclusive, this requires very little effort from hospital staff. Thus, healthcare providers should not overlook this consideration.
- The longer patients are under the effects of NMBA's, the higher the potential for debilitating side effects. This is especially true with ICU-acquired muscle weakness and corneal abrasions. If at all possible,



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

NMBAs should be given for the shortest amount of time possible. This decision should be made on a case-by-case basis by a specialist.

- Studies have shown that giving NMBAs slowly over the course of several minutes (1-3 minutes) can prevent histamine release. Conversely, a dose given too quickly can induce anaphylaxis.
- Because pancuronium has vagolytic action, it should not be the NMBA of choice in patients with coronary artery disease. These patients should receive vecuronium, as it has the least effect on the heart of any of the non-depolarizing NMBAs.
- Patients who are sensitive to vagolytics should not be given pancuronium or rocuronium.
- Patients who are sensitive to histamine-releasing effects should not be given atracurium.
- Patients who are given pancuronium are likely to experience tachycardia, and patients who are given vecuronium are likely to experience bradycardia.

References

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Upcoming Featured Topic for July/August Newsletter

Topic: Pain Management

Submission Date: July 10, 2017

Submit To: Barb Kasper kasperb@umkc.edu

If interested in submitting, please email Barb Kasper with the article title in advance to ensure availability

Future Newsletter Topics & Deadlines:

September 11th

Cardiology/Anticoagulation

November 13th

Infectious Diseases

SAVE THE DATE

MSHP & KCHP SPRING MEETING

May 4-5th, 2018

Embassy Suites

Olathe, Kansas



Missouri Society of Health-System Pharmacists Newsletter May/June 2017

MSHP Board of Directors

2017-2018

President	Jeremy Hampton	hamptonjp@umkc.edu
President-Elect	Tony Huke	Michael.Huke@tmcmcd.org
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2016-2017

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Questions/Comments

If you have any questions or comments about MSHP Newsletter, please don't hesitate to contact the Incoming Newsletter Chair, Barb Kasper, kasperb@umkc.edu 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!

Appendix A. Neuromuscular Blocking Agents

NMBA	Non-Depolarizing Agents					Depolarizing Agent
	Aminosteroids			Benzylisoquinoliniums		Succinylcholine
	Pancuronium	Vecuronium	Rocuronium	Atracurium	Cisatracurium	
MOA	Competitive antagonist at nicotinic receptors thereby inhibiting depolarization and preventing muscle contraction					Agonist at nicotinic receptors. Binds to acetylcholine receptors resulting in flaccid paralysis
Duration of Action	<i>Onset:</i> 3-5 minutes <i>Duration:</i> 60-90 minutes (Long-acting)	<i>Onset:</i> 3-5 minutes <i>Duration:</i> 40-60 minutes (Intermediate-acting)	<i>Onset:</i> 60-90 seconds <i>Duration:</i> 20-40 minutes (Intermediate-acting)	<i>Onset:</i> 3-5 minutes <i>Duration:</i> 20-40 minutes (intermediate-acting)	<i>Onset:</i> 2-3 minutes <i>Duration:</i> 30-60 minutes (intermediate-acting)	<i>Onset:</i> 30-60 seconds <i>Duration:</i> 3-5 minutes (Short-acting)
Metabolism	Renal and hepatic	Renal and hepatic	Renal and hepatic	Hoffman elimination	Hoffman elimination	Rapidly hydrolyzed by plasma pseudocholinesterase to inactive metabolites
Half-Life	1-2 hours	65-75 minutes	1.4-2.4 hours	20 minutes	22-29 minutes	----
Uses	<ul style="list-style-type: none"> • ICU paralysis 	<ul style="list-style-type: none"> • Surgical relaxation • ICU paralysis • Refractory shiver 	<ul style="list-style-type: none"> • RSI • Tracheal intubation • Control of shiver • ICU paralysis 	<ul style="list-style-type: none"> • Surgical anesthesia • ICU paralysis 	<ul style="list-style-type: none"> • Surgery • ICU paralysis • ARDS 	<ul style="list-style-type: none"> • RSI
Side Effects	<ul style="list-style-type: none"> • Tachycardia • Hypertension • Severe myasthenia (long-term use) • Sialorrhea 	<ul style="list-style-type: none"> • Anaphylactoid reaction (rare) • Prolonged paralysis • Flushing 	<ul style="list-style-type: none"> • Anaphylactoid reaction (rare) • Increased peripheral vascular resistance • Tachycardia 	<ul style="list-style-type: none"> • Flushing • Bradycardia • Bronchospasm • Hypotension 	<ul style="list-style-type: none"> • Bradycardia • Bronchospasm • Flushing 	<ul style="list-style-type: none"> • Bradycardia • Increase in serum potassium • Malignant hyperthermia
Clinical Pearls	<ul style="list-style-type: none"> • Caution with coronary artery disease • Active metabolite (~30-50% parent activity) 	<ul style="list-style-type: none"> • Less cardiovascular effects than other aminosteroids • Active metabolite (~50% parent activity) 	<ul style="list-style-type: none"> • Active metabolite (~5-10% parent activity) 	<ul style="list-style-type: none"> • Not prolonged with renal or hepatic dysfunction • Histamine release occurs 	<ul style="list-style-type: none"> • Not prolonged with renal or hepatic dysfunction • No histamine release 	<ul style="list-style-type: none"> • Controversial increase in intracranial pressure • Fasciculations precede paralysis • Avoid use with pre-existing hyperkalemia

Sustained Neuromuscular Blockade in the Adult Critically Ill Patient

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Appendix B. Non-Depolarizing Neuromuscular Blocker Reversal Agents

Reversal Agents	Physostigmine	Neostigmine	Edrophonium	Sugammadex
	Acetylcholinesterase Inhibitor			Modified cyclodextran
MOA	Inhibits destruction of acetylcholine by acetylcholinesterase resulting in increased cholinergic responses			Forms a complex with rocuronium or vecuronium in plasma, reducing the amount of neuromuscular-blocking agent available
Duration of Action	<i>Onset:</i> 3-8 minutes <i>Duration:</i> 45 to 60 minutes	<i>Onset:</i> 10-30 minutes <i>Duration:</i> 20-30 minutes	<i>Onset:</i> 30 to 60 seconds <i>Duration:</i> 10 minutes	<i>Onset:</i> < 3 minutes <i>Duration:</i> Dose dependent
Metabolism	Hydrolysis by cholinesterases	Hepatic	Unknown	Renal unchanged
Half-Life	1-2 hours	24-113 minutes	125 minutes	2 hours
Side Effects	<ul style="list-style-type: none"> • Bradycardia • Bronchoconstriction • Increased secretions • Urinary urgency • Hypersensitivity 			<ul style="list-style-type: none"> • Bradycardia • Anaphylaxis (rare) • Headache • Nausea and vomiting
Clinical Pearls	<ul style="list-style-type: none"> • IV formulations recommended for reversal indication • Use of antimuscarinics is recommended to mitigate the side effects of increasing acetylcholine at muscarinic sites (Ex: glycopyrrolate or atropine) • Use with caution in patients with preexisting rhythm issues, asthma, and myasthenia 			<ul style="list-style-type: none"> • Not recommended in patients with CrCl < 30 • Transient increase in aPTT • Interference with hormonal contraceptives possible

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