

Editors' Note: This issue contains a series of articles regarding the safe use of nondepolarizing neuromuscular blocking drugs. All anesthesia professionals should understand the importance of appropriately monitoring and reversing neuromuscular blockade. We believe that these articles will increase awareness, provide important educational information, and improve patient safety.

Monitoring of Neuromuscular Blockade: What Would You Expect If You Were the Patient?

by Robert K. Stoelting, MD

The Anesthesia Patient Safety Foundation (APSF) believes that residual neuromuscular blockade in the postoperative period is a patient safety hazard that could be addressed partially by better and consistent use of our qualitative standard train-of-four (TOF) nerve stimulator monitors, but will ultimately require quantitative (objective TOF) monitoring along with traditional subjective observations to eliminate this problem completely.¹⁻² APSF and other anesthesia professionals believe that every patient receiving nondepolarizing neuromuscular blocking drugs (NMBDs) should have at least qualitative, and preferably quantitative monitoring of the intensity of neuromuscular blockade using a peripheral nerve stimulator during the intraoperative period and assessment of the pharmacologic antagonism of neuromuscular blockade and adequacy of neuromuscular function prior to tracheal extubation.¹⁻¹⁰

Table 1: Potential adverse effects of residual neuromuscular blockade in the immediate postoperative period

Need for tracheal reintubation
Impaired oxygenation and ventilation (may be erroneously attributed to opioids)
Impaired pulmonary function (reduced forced vital capacity and peak expiratory flow rate)
Increased risk of aspiration and pneumonia
Pharyngeal dysfunction
Delayed discharge from the PACU

The peer review literature supports the conclusion that residual neuromuscular blockade in the immediate postoperative period is more common than appreciated. This weakness may contribute to adverse patient events (Table 1).³⁻⁹ Based on quantitative TOF monitoring as many as 40% of patients arriving in the PACU have evidence of residual neuromuscular blockade.^{4,9}

Despite the evidence in the peer review literature and a survey of anesthesia professionals in which 90% of respondents agreed that quantitative TOF monitoring should be used routinely for patients receiving nondepolarizing NMBDs prior to transfer to the PACU, quantitative measurements of drug-induced neuromuscular blockade and the

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Large Anesthesia/Practice Management Groups: How Can APSF Help Everyone Be Safer?

by Robert K. Stoelting, MD

On September 10, 2015, APSF invited representatives of large anesthesia and practice management groups to meet with members of the APSF executive committee to discuss mutually relevant anesthesia patient safety issues. The goal was to help APSF identify and implement patient safety initiatives of particular interest and value to the conference participants.

Thirty-six attendees representing 23 large anesthesia/practice management groups participated in the half-day session (Table 1). These 23 groups represented a wide geographical cross-section of the United States and a variety of practice models

that included all categories of anesthesia professionals. The American Society of Anesthesiologists, which has a committee on Large Group Practice, was represented by Daniel J. Cole, MD, President Elect, and Paul Pomerantz, CEO.

As an introduction to the conference, Robert K. Stoelting, MD, APSF President, reviewed past, current, and possible future APSF patient initiatives and provided "his view" of the three options available for APSF recommendations to become "best practices."

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Dr. Robert Stoelting, moderating.

We As Patients Would Expect Better

“Blockade Monitoring,” From Cover

adequacy of pharmacologic reversal have not been widely utilized by anesthesia professionals (Fig. 1).¹ Achievement of the goal of routine qualitative or quantitative monitoring using a peripheral nerve stimulator is difficult when the daily experiences of anesthesia professionals do not predictably demonstrate the existence of a problem that may occur well after the anesthesia professional has turned over care to another health care professional.⁴ Universal adoption of quantitative monitoring is further impeded by the limited availability of easy-to-use, reliable monitoring technology. Many anesthesia professionals continue to rely on clinical signs (head lift, hand grip, negative inspiratory force, tidal volume) that are insensitive indicators of residual skeletal muscle weakness and applicable only to awake patients. Likewise, reliance on visual/tactile assessment of the TOF (low sensitivity to detect fade) to titrate the effects and assess the pharmacologic reversal of nondepolarizing NMBD is an insensitive and unreliable monitoring technique. Though double-burst stimulation (DBS) and fade with 100 Hz tetanic stimulation significantly improve the ability to detect residual neuromuscular blockade over single twitch or TOF monitoring or clinical signs, these modalities of assessing neuromuscular blockade are inferior to methods of quantitative monitoring such as acceleromyography.¹⁰

A recommendation for routine qualitative or quantitative monitoring of neuromuscular blockade with peripheral nerve stimulators as part of the “Standards for Basic Anesthetic Monitoring” has not been promulgated by any of the North American professional anesthesia associations (American Society of Anesthesiologists, American Association of Nurse Anesthetists, American Academy of Anesthesiologist Assistants, Canadian Anesthesiologists’ Society). To date, these anesthesia professional associations are either silent regarding monitoring neuromuscular blockade or limit their statements to (1) “monitor neuromuscular response” [no specific quantitative monitor mentioned] or (2) a “peripheral nerve stimulator should be available when patients receive neuromuscular blockers.”

In contrast, the 2015 “Recommendations for standards of monitoring during anaesthesia and recovery” published by the Association of Anaesthetists of Great Britain and Ireland (AAGBI) mandates that “a peripheral nerve stimulator must be used whenever neuromuscular blocking drugs are given.”⁹ These recommendations also list a peripheral nerve stimulator (if neuromuscular blocking drugs are used) as part of the “minimum monitoring for anaesthesia” along with pulse oximetry and capnography.⁹ This AAGBI mandate reflects the increasing recognition of the role of NMBDs in adverse postoperative pulmonary events.

In my opinion, there is no compelling reason to ignore this evidence-based patient safety issue and the obvious change in practice (qualitative, or preferably quantitative/objective monitoring with peripheral nerve stimulators to guide pharmacologic drug reversal) that would likely reduce the risk of potential adverse physiologic effects of lin-

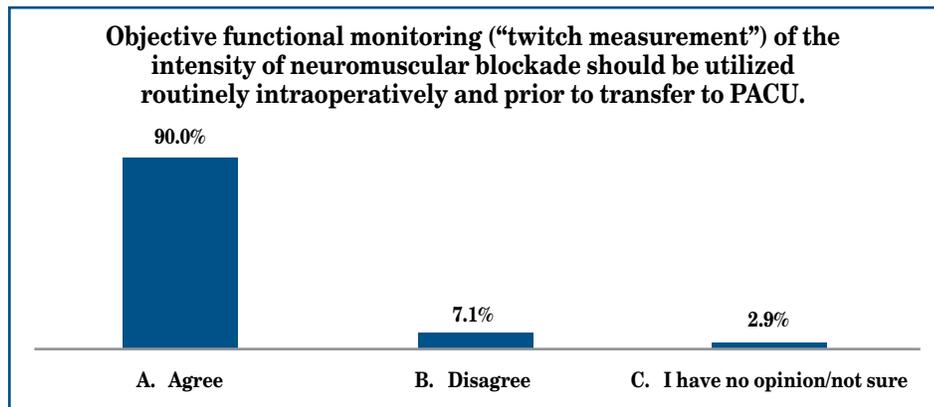


Figure 1: Stoelting RK. APSF survey results: Drug-induced muscle weakness in the postoperative period safety initiative. APSF Newsletter Winter 2013-14;28:69-71. <http://www.apsf.org/newsletters/pdf/winter2014.pdf>

gering drug-induced muscle weakness in the early postoperative period.

What will it take for “North American” anesthesia professionals to accept the reality of this patient safety risk?

Why are “we” so “hesitant” to routinely use qualitative or quantitative assessments of neuromuscular function with peripheral nerve stimulators to guide both the administration and reversal of nondepolarizing NMBDs?

Would “we,” knowing what we know, or should know, regarding the facts relevant to residual weakness due to nondepolarizing NMBDs, expect, at a minimum, qualitative monitoring with peripheral nerve stimulators if we were the patient?

My guess is “we” would expect qualitative, and more likely, quantitative monitoring of neuromuscular blockade as part of our care!

It is time to “Do as I would expect, not as I do!”

Robert K. Stoelting, MD
President, APSF

References

1. Stoelting RK. APSF survey results: Drug-induced muscle weakness in the postoperative period safety initiative. *APSF Newsletter* Winter 2013-14;28:69-71. Available at: <http://www.apsf.org/newsletters/pdf/winter2014.pdf>.
2. Stoelting RK. Residual drug-induced muscle weakness in the postoperative period—a patient safety issue. *ASA Newsletter* 2015;79:64-65. Available at: <http://www.asahq.org/search?q=February%202015%20ASA%20Newsletter>.
3. Brull SJ, Naguib M. What we know: Precise measurement leads to patient comfort and safety. *Anesthesiology* 2011;115:918-920.
4. Todd MM, Hindman BJ, King BJ. The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department. *Anesth Analg* 2014;119:323-331.
5. Viby-Mogensen J, Claudius C. Evidence-based management of neuromuscular block. *Anesth Analg* 2010;111:1-2.
6. Donati F. Neuromuscular monitoring: what evidence do we need to be convinced? *Anesth Analg* 2010;111:6-8.
7. Kopman AF. Managing neuromuscular block: where are the guidelines? *Anesth Analg* 2010;111:9-10.
8. Gopalaiah VK, Nair AP, Murthy HS, et al. Residual neuromuscular blockade affects postoperative pulmonary function. *Anesthesiology* 2012;117:1234-44.
9. Checketts MR, Alladi R, Ferguson K, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2015: Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia* 2015; Available at <https://www.aagbi.org/sites/default/files/Standards%20of%20monitoring%2020150812.pdf>
10. Capron F, Fortier LP, Racine S, Donati F. Tactile fade detection with hand or wrist stimulation using train-of-four, double-burst stimulation, 50-hertz tetanus, 100-hertz tetanus, and acceleromyography. *Anesth Analg* 2006 May;102:1578-84.



APSF-Sponsored Conference
Royal Palms Resort and Spa, Phoenix, AZ

Distractions in the Anesthesia Work Environment: Impact on Patient Safety

Distractions in the anesthesia work environment manifest in many different ways and potentially impact patient safety by compromising the anesthesia professional's vigilance during direct patient care. APSF believes these distractions need to be identified and addressed by open discussion, education, research and appropriate policy statements for individual groups or practice management entities. This 1-day conference will include podium presentations, panel discussions, small group breakout sessions and attendee responses using an “audience response system.”



Save the Date

Wednesday, September 7, 2016

If you are interested in attending, please contact Dr. Stoelting (stoelting@apsf.org) for registration details.

Residual NMB Remains Common Problem

“Neuromuscular Blockade,” From Preceding Page

regarding departmental progress; and the adoption of a TOF documentation requirement for our department's quarterly QI incentive bonus. Over the course of two months, two department-wide presentations (including a case conference) were devoted to a presentation of the data regarding the incidence and effects of residual paralysis. Attending anesthesiologists, CRNAs, and anesthesia resident champions were identified and designated as informational resources for questions and concerns. Furthermore, an online repository was created with links to the relevant literature in the field. The cognitive aid, a TOF-based neostigmine-dosing guide, was developed by one of our anesthesia residents (Matthew Meyer, MD) and distributed to the members of the department in an electronic format. It was also made available to them online and affixed to each anesthesia machine (Figure 1). Our department participates in a quarterly QI bonus program. As a “nudge” towards the adoption of better NMBD management practices, we tied the quarterly QI bonus to the rate of documentation of twitches within the fifteen minutes prior to the administration of neostigmine. Our goal was to provide a reminder to evaluate neuromuscular blocking reversal dosing in a manner that was not intrusive, easy to implement, and easy to monitor. The initiative has succeeded in improving the documentation of TOF. We are currently in the process of evaluating its effects on clinical outcomes.

We know that residual neuromuscular blockade is a relevant problem that leads to a significant increase in respiratory morbidity and health care utilization.^{8,12,20} However, residual neuromuscular blockade remains pervasive despite the advances in our understanding of this challenge since Dr. Viby-Mogensen's 1979 report. The fundamental issue appears to be the continued reliance by anesthesia professionals on informal and variable applications of qualitative clinical indicators rather than use of objective and quantitative TOF stimulation to determine appropriate reversal of neuromuscular blockade. The quantitative measurement of TOF stimulation is a reliable and objective measurement of adequate return of neuromuscular activity, and can be effectively used as a guide for appropriate neostigmine dosing. The QA/QI initiative at the MGH is an example of an integrated interdisciplinary approach by key stakeholders to promote sustained adoption of these best practices and improve patient safety. Broader adoption of similar evidenced-based initiatives and guidelines should provide a significant leap forward towards the elimination of the hidden universality of residual neuromuscular blockade and reduce the co-morbidities and added healthcare utilization associated with residual neuromuscular blockade.

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References

- Viby-Mogensen J, Jorgensen BC, Ording H. Residual curarization in the recovery room. *Anesthesiology* 1979;50(6):539-541.
- Eikermann M. The hidden universality of residual neuromuscular blockade. Letter to the Editor. Available at: <http://bj.a.oxfordjournals.org/letters/?first-index=11&hits=10&days=60>. Accessed 12/31/2015.
- Brull SJ, Murphy GS. "Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness." *Anesth Analg* 2010;111:129-140.
- Guidelines and Standards for Nurse Anesthesia Practice: Patient Monitoring Standards. American Association of Nurse Anesthetists 1992. Available at: https://www.aana.com/newsandjournal/Documents/patient_monitoring_0492_p137.pdf. Accessed 12/31/2015.
- Standards for Nurse Anesthesia Practice. American Association of Nurse Anesthetists 2013. Available at: <http://www.aana.com/resources2/professionalpractice/Documents/PPM%20Standards%20for%20Nurse%20Anesthesia%20Practice.pdf>. Accessed 12/31/2015.
- Stoelting, RK. APSF survey results: Drug-induced muscle weakness in the postoperative period safety initiative. *APSF Newsletter* 2013-14;28:49,70-71.
- Brueckmann B, Villa-Urbe JL, Bateman BT, et al. Development and validation of a score for prediction of postoperative respiratory complications. *Anesthesiology* 2013;118(6):1276-1285.
- Sasaki N, Meyer MJ, Malviya SA, et al. Effects of neostigmine reversal of nondepolarizing neuromuscular blocking agents on postoperative respiratory outcomes: a prospective study. *Anesthesiology* 2014;121(5):959-968.
- Martinez-Ubieto J, Ortega-Lucea S, Pascual-Bellota A, et al. Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reverted with neostigmine versus sugammadex. *Minerva anesthesiologica* 2015. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26472231>. Accessed 12/31/2015.
- Murphy GS, Szokol JW, Avram MJ, et al. Residual neuromuscular block in the elderly: Incidence and clinical implications. *Anesthesiology* 2015;123:1322-36.
- Murphy GS, Szokol JW, Marymont JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology* 2008;109:389-398.
- McLean DJ, Diaz-Gil D, Farhan HN, Ladha KS, Kurth T, Eikermann M. Dose-dependent association between intermediate-acting neuromuscular-blocking agents and postoperative respiratory complications. *Anesthesiology* 2015;122:1201-1213.
- Pavlin EG, Holle RH, Schoene RB. Recovery of airway protection compared with ventilation in humans after paralysis with curare. *Anesthesiology* 1989;70:381-385.
- Dam WH, Guldmann N. Inadequate postanesthetic ventilation. Curare, anesthetic, narcotic, diffusion hypoxia. *Anesthesiology* 1961;22:699-707.
- Bodman, RI. Evaluation of two synthetic curarizing agents in conscious volunteers. *Br J Pharmacol Chemother* 1952;7:409-416.
- Debaene B, Plaud B, Dilly M-P, Donati, F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *Anesthesiology* 2003;98:1042-1048.
- Murphy GS, Szokol JW. Monitoring neuromuscular blockade. *Int Anesthesiol Clin* 2004;42(2):25-40.
- Brull SJ, Prielipp RC. Reversal of neuromuscular blockade: "identification friend or foe." *Anesthesiology* 2015;122:1183-1185.
- Brueckmann B, Sasaki N, Grobara P, et al. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a randomized controlled study. *Br J Anaesth* 2015;115:743-751.
- Staehr-Rye AK, GS, Grabitz SD, Thevathasan T, Sasaki N, Meyer MJ, Gätke MG, Eikermann E. Effects of residual paralysis on postoperative pulmonary function and hospital length of stay. *ASA Abstract* 2015; A4026.



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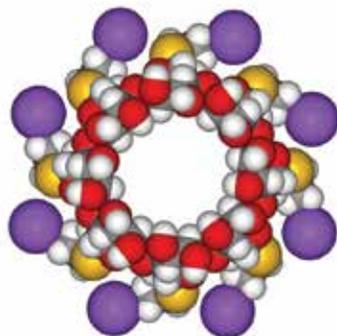
The Development and Regulatory History of Sugammadex in the United States

by Glenn Murphy, MD

The Neuromuscular Research Group at Organon Newhouse Scotland (east of Glasgow) had been working on the development of fast-onset, short-acting, nondepolarizing steroidal neuromuscular blocking agents since the 1960s, which led to the development of pancuronium, vecuronium and rocuronium. Shortly after the launch of rocuronium, questions arose about a possible action of rocuronium on smooth muscle neurotransmission, so Dr. Anton Bom was contacted. Dr. Bom was performing smooth muscle studies at the same research site. Rocuronium is not very water soluble, so buffer solutions with a pH of 4 are required. Dr. Bom attempted to dissolve rocuronium in organic solvents that were traditionally used for smooth muscle studies, none of which were able to solubilize rocuronium. Next, he decided to examine cyclodextrins, which were demonstrated to dissolve steroidal hormones. Cyclodextrins are rigid, ring-shaped molecules composed of sugar units. The outside of the cyclodextrin is hydrophilic, which makes the molecule water-soluble. The hole in the middle of the cyclodextrin ring is hydrophobic, which allows lipophilic molecules, like steroids, to enter this cavity, creating water-soluble complexes.¹

Since rocuronium has a steroidal nucleus, Dr. Bom speculated that rocuronium would form complexes with cyclodextrins. This binding would prevent rocuronium from acting on the nicotinic acetylcholine receptor and allow rapid reversal of neuromuscular blockade. His initial studies confirmed that rocuronium formed complexes with cyclodextrins. However, this binding was weak, allowing rocuronium to easily disassociate. Several modifications of the molecule were required to increase affinity. The cavity of the cyclodextrin was too small, so the cavity had to be extended by the addition of side-chains to each sugar unit. To ensure that the side-chains did not enter the cavity, negatively charged end-groups had to be attached to the side-chains. These modifications would allow a tight complex to form between the quaternary nitrogen of the rocuronium and the negatively charged ends of the side-chains. Dr. Ming Qiang Zhang, a medical chemist, then provided a long list of commercially available cyclodextrin molecules. The pharmacologists created in-vitro and in-vivo screening models, which allowed the creation of new cyclodextrin derivatives.¹

Sugammadex was developed to selectively bind to rocuronium. However, other steroidal muscle relaxants, such as vecuronium and pancuronium, are bound by sugammadex, but with a much lower affinity. There is no affinity of sugammadex for other classes of muscle relaxants (i.e. succinylcholine and the benzylisoquinoliums (mivacurium, atracurium and cisatracurium). One molecule of sugammadex is able to noncovalently bind one molecule of steroidal muscle relaxant.²



Space-filling model of sugammadex sodium.

In March of 1999, the first batch of Org 25969 (now known as sugammadex) was produced. In all pharmacological screening tests, this molecule showed the desired profile.

Both the concept of using modified cyclodextrins as reversal agents and the structure and synthesis of sugammadex and related cyclodextrins were patented in 2001. The first human study was performed in healthy volunteers and published in 2005.¹ This investigation demonstrated that 3 minutes after the administration of a normal intubation dose of rocuronium (0.6 mg/kg), 8 mg/kg of Org 25969 could completely reverse neuromuscular blockade. Since the publication of this initial investigation, sugammadex has been administered to over 6000 patients in clinical trials. In addition, sugammadex is approved in 57 countries, with approximately 11.5 million patients receiving the drug as of March 2015.¹

The first regulatory approval was in the European Union in 2008. In 2007, an application for approval to the FDA was submitted. In 2008, the FDA Advisory Committee unanimously recommended approval. However, the FDA issued a Not-Approvable Letter at this time. The FDA requested further characterization of sugammadex on repeat exposures due to concerns over hypersensitivity and anaphylactic reactions, as well as possible mechanistic causes of events. In the initial submission, there was one case of anaphylaxis and 31 cases of hypersensitivity. In addition, a small prolongation of aPTT and PT was noted in an in-vitro study.³ Further studies evaluating the effects of sugammadex on surgical bleeding were also requested. Finally, the need for additional studies examining the effects of sugammadex on cardiac arrhythmias and QT prolongation was noted.

In response to the FDA's requests, 4 additional studies were conducted examining the impact of sugammadex on coagulation. These investigations demonstrated a small increase in PT and aPTT that occurred within minutes of administration, but resolved within an hour. In addition, in a large

Safety Must Extend into Perioperative Period

“Expanding Influence,” From Page 48

undergoing procedures in body parts that have high concentrations of dwelling bacteria. Colorectal surgery is a good example.

Blood products contain much debris, including free hemoglobin and cellular stroma that can be toxic to organs such as kidneys. Processes that lead to reductions in blood transfusion are cost-effective, improve patient care in these settings, and help avoid prolonged disability, sepsis, and multi-organ failure. Approximately 40% of all blood products are transfused into surgical and procedural patients. The specialty is perfectly positioned to take lead roles in developing new algorithms or modifying existing algorithms for their specific practices and patient populations. In collaboration with transfusion medicine specialists, surgeons, and proceduralists, anesthesiologists and their care teams can work within health care settings to design and implement successful processes to reduce^{4,5} the use of blood products and decrease perioperative complications.

Human factors: Each step in a clinical pathway or process, whether it has been designed or occurred naturally, increases the opportunity for human error. Anesthesiologists, working closely with their health care colleagues and system engineers, can analyze, design, assess and continuously improve perioperative care pathways and processes by eliminating unnecessary steps. It is the right thing to do financially—reducing steps decreases expenses and increases efficiency. It is the right thing to do clinically—reducing steps decreases errors. It is the right thing to do for our patients—reducing steps decreases complications and increases patient safety.

Expansion of anesthesia care beyond intraoperative management and into an encompassing perioperative setting makes sense clinically because patients will benefit. It is another step forward in expanding the influence of the specialty in the safety of patients who are anesthetized for their surgical and procedural care.

Visionary leaders of the specialty during the past generation have noted that anesthesia care must evolve. Table 3 provides several of the quotes taken from selected ASA Rovenstine Lectures. These visionary colleagues had it right—expansion of the specialty to encompass perioperative care is necessary BECAUSE IT IS THE RIGHT THING TO DO FOR OUR PATIENTS.

I propose that the APSF reconsider its vision statement, “No patient shall be harmed by anesthesia.” It is now time that the statement should read, “No patient undergoing an anesthetic shall be harmed in the perioperative period.” This is the imperative you want to follow if you wish to expand the influence of the specialty into the future. This is the imperative you want to follow if you wish to have a greater influence on patient safety. This is the imperative you wish to have followed if you are the patient.”

Dr. Warner is Professor of Anesthesiology and Executive Dean at the Mayo Clinic College of Medicine in Rochester, Minnesota.

See “Sugammadex” Next Page

Sugammadex Approved After Multiple Delays

“Sugammadex” From Preceding Page

study of patients undergoing hip or knee replacement surgery, no increase in bleeding or transfusion requirements was observed in patients randomized to receive sugammadex.³ In order to address concerns related to cardiac arrhythmias, an analysis of phase 2 and 3 clinical studies was conducted, as well as an analysis of postmarketing data.^{4,5} These study findings indicated that QTc was not prolonged in patients given sugammadex. The studies also indicated that arrhythmias did not occur with greater frequency with sugammadex compared to neostigmine, although bradycardia can occur with both agents. Finally, a randomized, double-blind, placebo-controlled study in healthy volunteers was conducted to evaluate the incidence of allergic reactions to sugammadex.⁶

In 2012, another submission for approval was sent to the FDA. In 2013, a Complete Response Letter was provided to the sponsor. The FDA reported that protocol violations in the hypersensitivity study had been observed, which raised data reliability issues. However, bleeding and arrhythmia risks had been adequately addressed. In 2014, the sponsor resubmitted a new hypersensitivity trial in awake volunteers. A total of 375 awake subjects were given 3 intravenous doses of sugammadex (4 mg/kg, 16 mg/kg, or saline), and patients examined for hypersensitivity or anaphylactic reactions. One case met the criteria for anaphylaxis in the 16 mg/kg dose group (no hypotension or wheezing, treated with steroids and diphenhydramine), although the mechanism was unclear (no tryptase or IgG/IgE specific for sugammadex). Furthermore, no cases of anaphylaxis were reported in 3,519 patients administered sugammadex in clinical trials. Finally, in postmarketing data, 273 reports of anaphylaxis were reported in approximately 11.5 million sugammadex exposures, with 237 of 241 patients recovering with standard therapy.⁶

In 2015, a second Complete Response Letter was sent to the sponsor. At one site of the hypersensitivity study, staff who dosed subjects in one cohort performed adverse assessments in a different cohort. The FDA requested additional site inspections and sensitivity analysis. In November of 2015, the FDA again convened to review the resubmitted data. After review of all submitted studies as well as postmarketing data, the FDA Advisory Committee again unanimously recommended approval.⁷ Approximately 8 years after the initial FDA submission, sugammadex, owned and marketed by Merck, received FDA approval on December 16, 2015.

Sugammadex represents a novel and new drug, which offers several important advantages over current anticholinesterase reversal agents. Deep levels of neuromuscular blockade (train-of-four (TOF) count of 0, post-tetanic count of 1–2) can be reversed effectively with 4 mg/kg of sugammadex within 3 minutes, whereas neostigmine is ineffective in antagonizing deep blockade. At moderate levels of neuromuscular block (TOF count of 2), the mean time to achieve full recovery

(TOF ratio of 0.9) with sugammadex is 1.5 minutes versus 19 minutes with neostigmine.⁸ Furthermore, in urgent or emergent reversal of large doses of rocuronium (1.2 mg/kg), the mean time to neuromuscular recovery is significantly faster with sugammadex (16 mg/kg) compared to spontaneous recovery with succinylcholine.⁹ Sugammadex will allow increased flexibility of neuromuscular management in the operating room; deep blockade can be maintained until the end of surgery if required and then quickly reversed. Most importantly, the risk of residual neuromuscular blockade in the PACU can be significantly reduced if sugammadex is appropriately dosed. In the absence of consistent neuromuscular blockade monitoring with peripheral nerve stimulators and/or specified guidelines for reversal, recent data has demonstrated that the risk of residual block in the PACU can be reduced from 43% in patients given neostigmine to 0% in those given sugammadex.¹⁰ Finally, data from phase 1–3 clinical studies, volunteer subject investigations and post-marketing data in over 12 million patients have demonstrated that sugammadex is safe, with a rare risk of anaphylactic reactions that are treatable with standard therapy.⁷

The adoption of sugammadex by hospitals, pharmacies and anesthesia providers may be impacted by cost concerns. As with all newly FDA-approved drugs, anesthesia providers should be aware that post-marketing surveillance provides a vehicle for communicating with the FDA about any concerns of adverse events that may be associated with this new drug.

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References

1. Gijzenbergh F, Ramael S, Houwing N, van Iersel T. First human exposure of Org 25969, a novel agent to reverse the action of rocuronium bromide. *Anesthesiology* 2005;103:695–703.
2. Schaller SF, Fink H. Sugammadex as a reversal agent for neuromuscular block: an evidence-based review. *Core Evidence* 2013;8:57–67.
3. Rahe-Meyer N, Fennema H, Schulman S, Klimscha W, Przemek M, Blobner M, Wulf H, Speck M, McCrary Sisk C, Williams-Herman D, Woo T, Szegei A. Effect of reversal of neuromuscular blockade with sugammadex versus usual care on bleeding risk in a randomized study of surgical patients. *Anesthesiology* 2014;121:969–77.
4. de Kam PJ, Kuijk JV, Smeets J, Thomsen T, Peeters P. Sugammadex is not associated with QT/QTc prolongation: methodology aspects of an intravenous moxifloxacin-controlled thorough QT study. *Int J Clin Pharmacol Ther* 2012;50:595–604.
5. de Kam PJ, Grobara P, Dennie J, Cammu G, Ramael S, Jagt-Smook ML, van den Heuvel MW, Berg RJ, Peeters PA. Effect of sugammadex on QT/QTc interval prolongation when combined with QTc-prolonging sevoflurane or propofol anaesthesia. *Clin Drug Investig* 2013;33:545–551.
6. Merck Sharp & Dohme Corp. A study to evaluate the incidence of hypersensitivity after administration of sugammadex in healthy participants (MK-8616-101). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2014 Jan 13]. Available from: <http://clinicaltrials.gov/show/NCT02028065> NLM Identifier: NCT02028065.
7. Merck Sharp & Dohme Corp. NDA 22225: Sugammadex Injection Anesthetic and Analgesic Drug Products Advisory Committee (AC) Meeting: Sugammadex Advisory Committee Briefing Document, Kenilworth, NJ, November 6, 2015.
8. Blobner M, Eriksson LI, Scholz J, Mutsch J, Della Rocca G, Prins ME. Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: results of a randomised, controlled trial. *Eur J Anaesthesiol* 2010;27:874–81.
9. de Boer HD, Driessen JJ, Marcus MA, Kerckamp H, Heeringa M, Klimek M. Reversal of rocuronium-induced (1.2 mg/kg) profound neuromuscular block by sugammadex: a multicenter, dose-finding and safety study. *Anesthesiology* 2007; 107: 239–244.
10. Brueckmann B, Sasaki N, Grobara P, Li MK, Woo T, de Bie J, Maktabi M, Lee J, Kwo J, Pino R, Sabouri AS, McGovern F, Staehr-Rye AK, Eikermann M. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a randomized, controlled study. *BJA* 2015; 115: 743–751.



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EDITOR'S Q&A

How Do I Prepare for OR Power Failure?

by Erica L. Holland, MD; Carli D. Hoaglan, MD; Martha A. Carlstead, CRNA; Ryan P. Beecher, CRNA; Grete H. Porteous, MD

Introduction

Loss of electrical power in a hospital is a patient safety hazard that has been neglected in medical training and research.^{1,2} The technology-rich environment of the operating room (OR) puts patients at risk should a sudden loss of power occur, as lights and critical equipment may fail without warning. Regional disasters and extreme weather events are the most common causes of power outages. Extreme weather events have become more common in the past two decades, and it is projected that regional power failures will occur more frequently and last longer in future years, despite efforts to improve power grid resiliency.^{3,4} Hospital power failure may also be the result of a local disruption of municipal power, or be limited to a single institution. Published case reports (Appendix 1 on page 62) suggest that frequent root causes of intraoperative power loss are a failure of emergency generators to function during a widespread power outage, and hospital construction work that unmasks faults in internal electrical systems.⁵⁻¹¹ These reports underscore the fact that hospital emergency generators and back-up systems are not completely reliable. Anesthesia providers need to know as much about responding to power failure as they do about managing any other intraoperative crisis. As there is no centralized reporting system for hospital power failure events, the true incidence of this emergency is unknown. Based on anecdotal experience, we believe it may be more common than is generally appreciated.

In addition to direct effects on critical anesthesia equipment, other repercussions of power outage in the OR can be extensive (Table 1). Power failure often translates to loss of lighting in the OR and adjacent hallways. Surgeons are faced with loss of electrosurgical units, video display monitors, and suction.^{6,8} Anesthesia machines and ventilators revert to battery power, which may last from 30 to 90 minutes depending on device and manufacturer specifications. Surprisingly, there are few reports on how well anesthesia machines function on battery power, and what can be expected when

Table 1. Vulnerability of operating room equipment and hospital services to power failure

This table is intended as an overview, as actual equipment performance may vary based on institution and make and model of device. Devices with limited or no battery back-up should operate if plugged into an emergency circuit ("red outlet") and generators are working.

Substantial battery back-up, or not dependent on electrical power	
Anesthesia machine/ventilator	Portable ultrasound machines
Non-desflurane vaporizers	Intra-aortic balloon pump
Portable patient monitors	Laptop computers
Portable infusion pumps	Medical gases (e.g., pipeline oxygen)
Portable suction	
Limited or no battery back-up	
Room lights	Patient warming devices
End-tidal gas analyzer	Transesophageal echocardiography machines
Automated medication dispensing devices (e.g., Cerner's RxStation®)	Wall suction and scavenging systems
Desflurane vaporizer	Da Vinci® Surgical System*
Patient monitors without battery back-up	Video towers
Electrosurgical units	Cardiopulmonary bypass machine
Fluoroscopy/portable X-ray units	Desktop computers without battery
Fluid warmers/rapid infusion devices	Cell salvage machine
Depends on institution	
WiFi/Internet access	Badge-activated door locks
Paging systems	Electronic medical record
Telephones	

*Battery allows undocking of patient from robot.

their batteries are finally depleted. Electronic patient monitors, desflurane vaporizers, and end-tidal gas analyzers often lack battery back-up. Hospital power failure may compromise communications (telephones, pagers, WiFi), electronic medical records, access to critical medications from automated dispensing cabinets, room temperature control, sterilization capabilities, elevators, and staff access to clinical areas through badge-secured doors.^{12,13} In some cases, operations may need to be aborted and patients evacuated. Prolonged hospital power failure eventually impacts sanitation, access to food and clean water, transportation and security.

Our anesthesia department at a tertiary-care medical center was recently faced with the challenge of preparing for electrical upgrades in a new hospital building that could temporarily compromise emergency generator power delivery to a suite of operating rooms and other critical areas. Published reports suggest that anesthesia departments should be knowledgeable about the battery life and capabilities of their equipment, should have sources of back-up lighting and monitoring immediately available, and should have a disaster plan that engages the entire OR staff. We thus embarked upon a project to review our current emergency plans, test the functionality of key anesthesia equipment during

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power failure, and develop a safety checklist and inexpensive emergency patient monitoring kit.

Anesthesia Equipment Testing

We tested two different anesthesia machines, one portable monitor and one infusion pump for duration of battery life and functionality on battery power (Table 2). Multiple examples of each device were tested, and all devices were charged overnight prior to testing. Anesthesia machine, ventilator, infusion pump, and portable monitor function were observed until display screens indicated “0% battery,” and then until devices failed and screens became dark.

We found that all types of equipment had a battery life longer than expected, approximately 3 to 4 hours. Anesthesia machine battery life was extended by approximately 1 hour by turning the ventilator off and using manual ventilation. Ventilators on Fabius machines continued to operate for <10 minutes after “0% battery” was displayed, but Apollo ventilators continued functioning for several hours longer. Sevoflurane vaporizer output on both types of anesthesia machines was consistent with dialed settings as long as there was fresh gas flow, and did not depend whether the anesthesia machine was using alternating current (AC) power, battery power, or had a completely depleted battery. Fresh gas flow, rotometers, and the oxygen flush valve were unaffected by AC power loss or battery depletion. These observations are consistent with the manufacturer’s specifications, except that battery life was consistently longer than the 30–90 minutes advertised for these machines (Dräger anesthesia machine user manuals courtesy of Dräger Medical, Inc). Alaris pumps failed within minutes of “battery failure” warning screens. Their fluid volume output was no different whether on battery or AC power. Phillips monitors also failed within about 15 minutes of a “0% battery” indicator screen. In general, displays on all devices underestimated actual battery life. It is unsurprising that manufacturers err on the side of caution in displaying this value to the user, particularly for critical medical devices. All types of devices displayed increasingly loud, visible, and difficult-to-ignore warnings when close to battery failure (Figure 1). No device failed without warning during testing. It is important to note that complete battery depletion during tests such as these can adversely affect subsequent battery function, so repeated tests are not advised.

Table 2. Results of anesthesia equipment testing

Device	Testing mode	Devices Tested	Hours to “0% battery” display Mean (Range)
Dräger Apollo® anesthesia machine	Ventilator on	2	4.8 (4.3–5.5)
	Ventilator off	1	5.6
Dräger Fabius® anesthesia machine	Ventilator on	2	3.5 (3.2–3.7)
	Ventilator off	2	4.6 (4.4–4.8)
Phillips IntelliVue x2® portable monitors	With BP cuff	3	3.0 (2.6–3.6)
	Without BP cuff	1	3.4
Alaris PC® infusion pumps	2 channels	4	4.2 (3.9–4.5)

Anesthesia machines on battery power were tested both with ventilator on (set to tidal volume of 500 mL and respiratory rate 10 breaths per minute), or ventilator off (simulating a “manual ventilation” state). Fresh gas flow was set to 2 L/min, sevoflurane was dialed to 2%, and end-tidal sevoflurane was measured. Alaris pumps were set-up to run two channels, simulating a carrier infusion at 150 mL/hour and a phenylephrine infusion at 25 mcg/min. In addition to measuring infusion pump battery life, the function of infusion pumps was measured by comparing pump output in mL/hour for devices on battery power compared to alternating current (AC) power. Phillips monitors were tested for battery life both with a non-invasive blood pressure (NIBP) cuff cycling every 5 minutes, and with no NIBP cuff measurements.

Emergency Monitoring Supplies

While it is helpful to know how anesthesia equipment will generally perform during a crisis, it is also wise to plan for contingencies. In order to be prepared for a worst-case scenario in which patient monitors fail and portable monitors are unavailable, we designed and distributed “Emergency Monitoring Kits” to carts in every anesthetizing location. Figure 2 shows the contents of the \$60 kits, of which the most important are an inexpensive pulse oximeter and a light-emitting diode (LED) headlamp.

The kits are sealed with break-away tags to discourage component theft, and batteries in headlamps, pulse oximeters, and LED flashlights kept in all anesthesia machines are replaced every 6 months. A paper anesthetic record is included not only for anesthesia charting, but as a critical part of patient identification and documentation during an evacuation.

OR Power Failure Checklist

Checklists are useful cognitive aids for clinicians that have been proven to increase patient

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Figure 1. Screens displayed on Dräger Apollo and Fabius GS anesthesia machines at time of battery failure.

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safety in numerous areas of medicine.^{14,15} For anesthesiologists and nurse anesthetists, checklists are particularly helpful guides for patient management during rare, life-threatening intraoperative events such as malignant hyperthermia and local anesthetic systemic toxicity.¹⁶⁻¹⁸ In published reports, anesthesia providers have had variable responses to operating room power failure, including switching to manual ventilation and discontinuing volatile anesthetics.^{6,7} These actions may be appropriate in some power failure situations, and inappropriate in others.

As we were unable to find any published checklists on crisis management for OR power failure, we created our own (Figure 3). Based upon the results of equipment testing and multiple simulations, we decided that the crucial first step during power failure was to determine whether the anesthesia machine and ventilator were functional, and if so, to continue using them. This step allows the clinician's hands to be free to perform other necessary tasks, allows continued delivery of a reliable anesthetic, and minimizes the chance of barotrauma and respiratory alkalosis from manual ventilation. Confidence that volatile anesthetic will continue to be delivered removes the immediate burden on the anesthesia provider to urgently convert to a total intravenous anesthetic (TIVA) in the dark. Furthermore, as electronically controlled medication dispensing stations are not operational without power, supply of intravenous sedatives and anesthetics may be rapidly depleted if multiple ORs are affected. Another crucial element of the checklist involves repeated steps to assure the delivery of oxygen to the patient. In the case of a disaster such as an earthquake, pipeline oxygen supply may be damaged or turned off as a fire control measure. We also include prompts for the anesthesia provider to confirm that critical equipment is plugged into a generator-powered circuit (“red outlets”), to communicate with the surgical team and nursing staff regarding prioritization of help for patient care, and to prepare for patient evacuation if necessary.

Discussion

Operating room power failure is a critical event that merits advance preparation to prevent catastrophic patient harm. Hospitals are rightly subject to rigorous regulations regarding emergency generator power testing and reliability, and required to develop plans for power failure emergencies.¹⁹ In most cases, it is likely that in the event of intraoperative power loss, approximately 10 seconds (or longer) of darkness will be followed by restoration of power by generators. Return of electrical power does not

mean the end of a crisis, however, as sophisticated medical equipment may be damaged by power surges or forced to undergo a prolonged restarting process. Recently at our institution, municipal power interruption of less than a second caused by an accident at a local electrical substation resulted in unanticipated problems: damage to delicate electronics in some fluoroscopy equipment, malfunction of a transesophageal echocardiography machine during a cardiac case, and loss of video imaging for several minutes during a da Vinci[®] robot-assisted laparoscopic case in which significant bleeding was occurring. A delay of care for several minutes as equipment reboots during a critical part of a procedure can be dangerous. Regardless of whether a crisis is brief or prolonged, or whether generators work or not, patients remain at significant risk whenever power is interrupted.

Management of intraoperative power failure should be part of a coordinated medical facility response. While preparedness within the operating room is important, it is equally important to develop an institutional system for disaster response that allows for a clear chain of command with recognized roles and protocols, rapid assessment of patient needs, and deployment of resources. The Hospital Incident Command System (HICS)²⁰ is the basis of our institution's efforts to build a robust emergency preparedness program. Within the HICS system, protocols in perioperative areas are being developed that allow staff to rapidly assess operating room needs and triage care even in the presence of darkness and loss of normal avenues of communication. Individual operating room needs are triaged by color to direct assistance to the most critical, and gauge

OR readiness to receive patients during an emergency.

This project has allowed us to explore our capabilities “in the dark” as an anesthesia service practicing in an earthquake hazard area, and has also allowed us to engage the entire medical center in preparations and simulations for disaster planning. Anesthesiologists, nurse anesthetists, and anesthesia technicians should learn about the battery capabilities of their equipment and the projected impact of a power outage on key services necessary for patient care. Anesthesia departments should have extra equipment for patient monitoring readily available, most importantly, LED headlamps and battery-powered pulse oximeters. A checklist may help clinicians remember to perform key steps when the lights go out: finding alternative light sources, preventing hypoxemia, and confirming that critical equipment is plugged into generator-powered outlets. We continue to refine and practice this checklist and our disaster response protocols, and hope that others may use our experience as a starting point for discussing preparedness for power failure and other emergencies at their own institutions.

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Figure 2. Emergency patient monitoring kits. Kits contain an LED headlamp, sphygmomanometer, stethoscope, pulse oximeter, colorimetric CO₂ detector, paper anesthetic record, and copy of the power failure emergency checklist.

Power Out?

Is Ventilator Still Working?

YES

Call for HELP while doing the following...

- Continue normal use of ventilator & non-desflurane vaporizers
- Change FiO₂ to 100% @ 2 L/min

NO

Call for HELP while doing the following...

- Adjust APL and manually ventilate utilizing pipeline O₂ or E-cylinder @ 100% FiO₂
- O₂ flush valve may need to be pressed multiple times to refill circuit to manually ventilate
- O₂ flowmeter & O₂ flush valve will still function
- Non-desflurane vaporizer will still function at approximate dialed setting

- Obtain additional light source if not already done (e.g., flashlight, headlamp, laryngoscope, cell phone)
- Open emergency monitoring kit in bottom drawer of anesthesia cart. Apply manual patient monitors (pulse ox, NIBP). Listen for breath sounds, use colorimetric CO₂ detector as needed.
 - o If available, use portable transport/"brick" monitors
 - o Check patient vital signs and chart every 5 minutes on paper anesthetic record
- Confirm Ambu-bag available and O₂ E-cylinder on back of anesthesia machine is at 2000 psi
 - o If pipeline O₂ fails, utilize O₂ E-cylinder on back of machine
 - o Anticipate possible need to switch to Ambu-bag with auxiliary O₂ tank or room air
- Notify anesthesia attending, anesthesia tech, & charge anesthesiologist of situation
- Communicate with surgical team regarding status & determine patient triage category: Red, Yellow, Green, Blue, or Black (see "Patient Triage Guidelines" in binder)
- Confirm that critical room equipment is plugged into RED outlets
- Obtain additional propofol, opioids, and midazolam, if needed
- Maintain 100% FiO₂ at 2 L/min unless contraindicated
- Anticipate possible upcoming need for IV anesthesia (see "Quick Propofol Drip Guide" in binder)
- Prepare for possible patient evacuation (see "Patient Evacuation Kit" in binder)
- Anticipate that anesthesia machine battery and Alaris pumps may last as long as 3 hours (not guaranteed)
 - o Consider transition from controlled to spontaneous ventilation to conserve battery

TROUBLESHOOTING VENTILATOR

- If ventilator fails to operate, try turning machine Off/On
 - o Fabius switch location: back lower right corner (Figure 4)
 - o Apollo switch location: front lower right corner, hold for 3 sec (Figure 5)
- Attempt to plug ventilator into different red outlet
- If difficulties manually ventilating, try pressing O₂ flush valve several times to fill circuit

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Figure 4: Fabius On/Off Switch (back of machine).

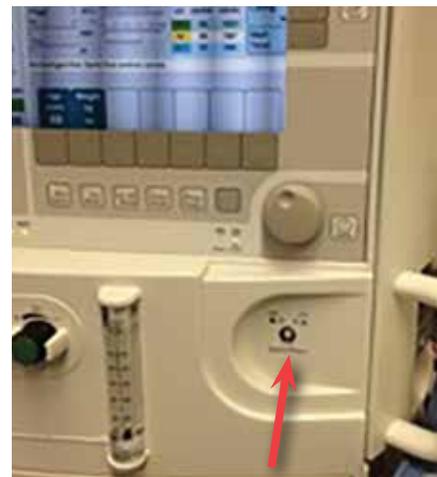


Figure 5: Apollo On/Off Switch (hold for 3 sec).

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References

1. Eichhorn JH, Hessel EA. Electrical power failure in the operating room: a neglected topic in anesthesia safety. *Anesth Analg* 2010;110:1519-21.
2. Klinger C, Landeg O, Murray V. Power outages, extreme events and health: a systematic review of the literature from 2011-2012. *PLoS Curr* 2014 Jan 2; 6:ecurrents.dis.04eb1dc5e73dd1377e05a10e9edde673
3. Larsen PH, LaCommare KH, Eto JH, Sweeney JL. Assessing changes in the reliability of the U.S. electric power system. Lawrence Berkeley National Laboratory 2015. Available at: <https://publications.lbl.gov/islandora/object/ir%3A188741>. Accessed October 20, 2015.
4. DOE-PI (U.S. Department of Energy's Office of Policy and International Affairs): U.S. Energy sector vulnerabilities to climate change and extreme weather. 2013.

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- Available at: <http://energy.gov/sites/prod/files/2013/07/12/20130710-Energy-Sector-Vulnerabilities-Report.pdf>. Accessed October 20, 2015.
- Riley RH. Power failure to a tertiary hospital’s operating suite. *Anaesth Intensive Care* 2010; 58:785.
 - Carpenter T, Robinson ST. Response to a partial power failure in the operating room. *Anesth Analg* 2010; 110:1644-6.
 - Yasny J, Soffer R. A case of a power failure in the operating room. *Anesth Prog* 2005; 52:65-69.
 - Pagán A, Curty R, Rodriguez MI, Pryor F. Emergency—Total power outage in the OR. *AORN J* 2001; 74:514-516.
 - Tye JC, Chamley D. Complete power failure. *Anaesthesia* 2000; 55:1133-1134.
 - Troianos, CA. Complete electrical failure during cardiopulmonary bypass. *Anesthesiology* 1995; 82:298-302.
 - Norcross DE, Elliott BM, Adams DB, Crawford FA. Impact of a major hurricane on surgical service in a university hospital. *Am Surg* 1993; 59:28-33.
 - Nates JL. Combined external and internal hospital disaster: Impact and response in a Houston trauma center intensive care unit. *Crit Care Med* 2004; 32:686-690.
 - O’Hara JF, Higgins TL. Total electrical power failure in a cardiothoracic intensive care unit. *Crit Care Med* 1992; 20:840-845.
 - Treadwell JR, Lucas S, Tsou AY. Surgical checklists: a systematic review of impacts and implementation. *BMJ Qual Saf* 2014; 4:299-318.
 - Byrnes MC, Schuerer DJE, Schallom ME, et al. Implementation of a mandatory checklist of protocols and objectives improves compliance with a wide range of evidence-based intensive care unit practices. *Crit Care Med* 2009; 10: 2775-81.
 - Ziewacz JE, Arriage AF, Bader AM, et al. Crisis checklists for the operating room: development and pilot testing. *J Am Coll Surg* 2011; 213:212-19.
 - Neal JM, Mulroy MF, Weinberg GL. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. *Reg Anesth Pain Med* 2012; 37(1):16-8.
 - Harrison TK, Manser T, Howard SK, Gaba DM. Use of cognitive aids in a simulated anesthetic crisis. *Anesth Analg* 2006; 103(3):551-6.
 - JCAHO (Joint Commission on Accreditation of Healthcare Organizations): Preventing adverse events caused by emergency electrical power system failures. The Joint Commission Sentinel Event Alert 2006; 37: 1-3. Available at: http://www.jointcommission.org/sentinel_event_alert_issue_37_preventing_adverse_events_caused_by_emergency_electrical_power_system_failures/. Accessed October 20, 2015.
 - Arnold JL, Dembry LM, Tsai MC, et al. Recommended modifications and applications of the Hospital Emergency Incident Command System for hospital emergency management. *Prehosp Disast Med* 2005; 20(5):290-300.

Supplemental Materials

PATIENT TRIAGE GUIDELINES

Red	Needs immediate help and/or evacuation within 30 minutes, unstable patient, mechanically ventilated (outside of OR environment), or requiring significant cardiac or pulmonary resuscitation
Yellow	Can wait 30 min–2 hr for evacuation, relatively stable patient but requiring ongoing supportive care or continuation of procedure beyond 30 min
Green	Can abort or finish procedure within 30 min...OR...can wait > 2 hr for evacuation, patient otherwise stable
Blue	Can be discharged home within 30 min, stable patient
Black	Deceased

Quick Propofol Drip Guide

(To Approximate 100 mcg/kg/min)

Route	50 kg Patient	100 kg Patient
Intermittent Syringe Bolus	2.5 ml every 5 min	5 ml every 5 min
Mini-drip (60 drop/ml)	1 drop every other second	1 drop every second

PATIENT EVACUATION KIT

<input type="checkbox"/> Ambu-Bag	<input type="checkbox"/> Manual Monitors	<input type="checkbox"/> Propofol
<input type="checkbox"/> Mask	<input type="checkbox"/> Full O ₂ Tank	<input type="checkbox"/> Midazolam/Opioid
<input type="checkbox"/> Emergency Binder	<input type="checkbox"/> Extra Gloves	<input type="checkbox"/> Muscle Relaxant
<input type="checkbox"/> Oral Airway	<input type="checkbox"/> Extra IV Fluids	<input type="checkbox"/> Phenylephrine
<input type="checkbox"/> LMA #4	<input type="checkbox"/> Extra Syringes	<input type="checkbox"/> Ephedrine
<input type="checkbox"/> ETT/Stylet	<input type="checkbox"/> Extra Needles	<input type="checkbox"/> Atropine
<input type="checkbox"/> Laryngoscope	<input type="checkbox"/> Tape	<input type="checkbox"/> Code Epinephrine Box (100 mcg/ml)

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EDITOR'S Q&A

Appendix 1. Reports of intraoperative power failure. Abbreviations: OR – operating room; PACU – post-anesthesia care unit; ESU – electrosurgical unit; ICU – intensive care unit; CABG – coronary artery bypass graft; CPB – cardiopulmonary bypass; ACT – activated clotting time; TOF – train-of-four; TIVA – total intravenous anesthesia.
[†]Year of publication.

Year [†]	Scenario	Root Cause	Outcome	Recommendations
2010	<ul style="list-style-type: none"> Complete loss of power on two consecutive days 9 operations in progress Outage lasted 13 minutes on day 1 and 9 minutes on day 2 	<ul style="list-style-type: none"> Fault within the switching panel that controlled whether the hospital used municipal power or emergency generator power Unclear if generators worked 	<ul style="list-style-type: none"> Anesthesia monitors failed and “clinical monitoring” was used until portable transport monitors arrived Video towers and imaging systems failed Surgical lights, ventilators, gas delivery systems and CPB continued because of built-in batteries 	<ul style="list-style-type: none"> An uninterruptible power supply system for the OR should be installed as this would allow at least one hour of power in the ORs in order to complete ongoing procedures Staff should be familiar with power requirements of equipment⁵
2010	<ul style="list-style-type: none"> Partial hospital power failure with loss of power to emergency (generator) system 8 operations in progress, including a craniotomy, Whipple procedure, and kidney transplant Outage lasted 15 minutes 	<ul style="list-style-type: none"> During construction, a phase loss relay in main hospital circuit became dislodged, simulating loss of municipal power A critical branch transfer switch then connected hospital power to an emergency generator that was disabled for servicing “Red outlets” that were supplied by generator lost power 	<ul style="list-style-type: none"> Most anesthesia providers switched to manual ventilation, while two continued to use the battery-powered anesthesia machine ventilator 3 providers switched from desflurane to sevoflurane or isoflurane. One switched to propofol infusion with midazolam All patient monitoring was interrupted except in the one room where anesthesia equipment was erroneously not plugged into red outlet. Portable monitors were brought into rooms Room lights continued to function except in one room ESUs and automated drug supply cabinets failed 	<ul style="list-style-type: none"> Communication should be improved by notifying staff of potential power loss during possible service interruption and developing a “batch paging” system to notify key personnel during an emergency Anesthesia providers should focus on “ABCs”, call for help, utilize emergency equipment and ensure delivery of anesthesia to the patient All rooms should have portable backup lights If some equipment is functional in a room, consider plugging failed equipment into different outlets Phase loss relay component should be secured to avoid a similar accident in future⁶
2005	<ul style="list-style-type: none"> Complete loss of hospital power Emergency generators failed in wing of hospital with operating room, but functioned elsewhere Complex oral and maxillo-facial operation in progress Outage lasted days 	<ul style="list-style-type: none"> Multistate power outage (Northeast blackout of 2003) 	<ul style="list-style-type: none"> Room lights failed Anesthesia machine display and monitors worked, but ventilator bellows could not be seen in the dark TIVA initiated. Patient ventilated with self-inflating resuscitation bag and tank oxygen Once portable lights confirmed normal bellows function and pipeline gas supply, anesthesia machine resumed ventilation with volatile agent Operation was suspended, patient was left intubated and transported to PACU Operation completed the next day in a different building which had generator power 	<ul style="list-style-type: none"> Anesthesiologists have a critical leadership role in the OR during crisis. Clear communication and thoughtful planning are key to avoiding panic Daily equipment checks should include flashlights and batteries in every room The battery life of anesthesia equipment should be determined Consider resuming spontaneous ventilation under anesthesia as a safety precaution in case anesthesia machine battery fails⁷
2001	<ul style="list-style-type: none"> Complete loss of hospital power 3 operations in progress: ankle fusion, pelvic extension, and radical neck dissection Outage lasted >1 week, requiring evacuation of all hospital patients 	<ul style="list-style-type: none"> Fire in electrical vault Electricity still supplied to building by municipal power but unable to be distributed throughout hospital Main and backup generators destroyed by fire 	<ul style="list-style-type: none"> Flashlight used for light source in ORs Anesthesia machines continued to function on battery Wall suction failed and portable suction unit used Electrosurgical units failed and battery-powered bipolar eye electrosurgery units and vessel ligation were used to achieve hemostasis Automated drug supply cabinets failed All operative procedures were near completion and incisions were closed 	<ul style="list-style-type: none"> Create emergency staffing plan that identifies specific staff member responsibilities and roles Battery operated ESUs and suction should be available Perform mock disaster drills quarterly Pharmacy services should have a plan to ensure availability of medications to operating rooms Flashlights and paper intraoperative records should be available in ORs⁸
2000	<ul style="list-style-type: none"> Complete loss of hospital power Both emergency generators failed Carotid endarterectomy in progress Outage lasted 30 minutes 	<ul style="list-style-type: none"> Construction workers accidentally drove a steel pile through the hospital’s main incoming power cables The first generator did not start at all. The second generator started, but was quickly overloaded and then failed 	<ul style="list-style-type: none"> Room lights failed except for one light with a back-up battery Anesthesia machine ventilator continued to function Patient monitors failed, including gas analyzer and capnography. Surgeon watched pulsations of the carotid artery until a portable monitor was available Capnography and agent monitoring remained unavailable The case was aborted, and the patient was taken to the ICU 	<ul style="list-style-type: none"> Emergency generator planning should take into account the load placed on one generator in case a second generator fails⁹
1995	<ul style="list-style-type: none"> Complete loss of hospital power Ongoing cardiac case with patient on CPB Outage lasted 53 minutes 	<ul style="list-style-type: none"> Loss of municipal power during heat wave Emergency generators started, then failed after 15 minutes 	<ul style="list-style-type: none"> Room lights, CPB machine, communications (intercom, pager), patient monitors, and suction failed Roller head in CPB circuit was manually cranked to maintain a venous saturation > 70% Flashlights and laryngoscope lights were used for illumination Portable monitors and suction brought to room Measurement of ACT performed manually with flashlight and stopwatch Not possible to rewarm patient. Came off CPB on dopamine. CPB reinstated when power restored 	<ul style="list-style-type: none"> Hand-cranking a CPB machine is exhausting, and relief staff must be brought in for this purpose immediately The capabilities of various functions of the CPB machine and battery life must be determined in advance of a crisis When communications fail, all available anesthesia personnel should systematically check each OR to determine priority needs Battery powered lighting in hallways, workrooms and PACU is also necessary to find equipment and prevent staff injury Staff in ORs must be assessed periodically for heat exhaustion when air conditioning fails during a heat wave¹⁰
1993	<ul style="list-style-type: none"> Operating room loss of power. No mention of other hospital areas Ongoing laparotomy Emergency generators worked for approximately 3 minutes, then failed Outage lasted 45 minutes 	<ul style="list-style-type: none"> Regional power outage (likely Hurricane Hugo) Generator cooling system had been accidentally deactivated. When the generator activated in response to the power failure, it quickly overheated and failed 	<ul style="list-style-type: none"> All lighting, ventilator and monitors except for pulse oximeter failed Ventilation was continued manually via anesthetic circle system Portable monitors were used, including manual BP cuff, esophageal stethoscope, TOF monitor, oxygen analyzer, pulse oximeter and EKG Flashlights used, but inadequate for continuation of surgery. When power returned 45 min later, surgery resumed 	<ul style="list-style-type: none"> Clinicians should be ready to use manual monitors and physical exam to monitor patients if battery-powered devices fail Develop a plan for OR power outage and rehearse it¹¹

Residual Neuromuscular Blockade (NMB), Reversal, and Perioperative Outcomes

by Karl E. Hammermeister, MD; Michael Bronsert, PhD; Joshua S. Richman, MD, PhD; and William G. Henderson, PhD

Historical

The earliest description of curare, a naturally occurring predecessor of the neuromuscular blocking agents commonly used today in anesthesia, has been attributed to Sir Walter Raleigh in his 1596 book, *The Discoverie of the Large, Rich, and Beautiful Empire of Guiana*, in which he describes, "the most strong poyson on their arrows" used by an indigenous tribe of Guiana.¹ However, Ibanez cites numerous descriptions by Spanish explorers of lethally tipped arrows used by natives of northern South America in the century preceding the publication of Raleigh's book.²

Although Ibanez also describes therapeutic uses of what may have been curare, it was not until 1932 that West described experiments in patients with rigidity disorders at the Hospital for Epilepsy and Paralysis in Maida Vale, London; he concluded, (there was) "a definite, measurable reduction in the muscular rigidity resulting from diseases of the pyramidal and extrapyramidal motor system...[at] doses which produce no detectable signs of weakness."³ An early therapeutic use in humans to prevent fractures occurring with convulsive therapy for depression was described by Bennett in 1940.⁴ The earliest description of the use of curare in general anesthesia to achieve muscle relaxation during surgery we have found was at the Homeopathic Hospital of Montreal by Griffith, published in 1942.⁵ In 1954, Beecher and Todd, both at Harvard and the Massachusetts General Hospital, reported their massive study of 599,548 anesthetics in 10 university hospitals in the U.S. between 1948 and 1952.⁶ They undertook this study because of their, "...belief that anesthesia has an unnecessarily high death rate." All deaths were classified by a surgeon and anesthesiologist at each hospital; however, precise criteria for cause of death were not provided. A muscle relaxant was used in 2.8% (16,560), which

was tubocurarine in 55%, decamethonium bromide in 37%, and succinylcholine in 4% of cases. They found 6 times as many anesthetic deaths were associated with "curare," compared to patients managed without. Recognizing the need for risk-adjustment, 13,204 patients sampled in 1952 were classified as "good or poor physical status" (this was not the ASA classification, which had been published in 1941,⁷ but rather a seven-point scale devised by the authors, which was effectively similar to the ASA classification). The distribution of this scale was similar between patients receiving a NMB and those not.

Contemporary Studies

Residual NMB postoperatively has been known for more than 35 years,⁸ and occurs commonly despite reversal with neostigmine with a reported incidence of 4 to 50%.^{9,10} Studies prior to 2005, suggested residual neuromuscular block should be defined by a train-of-four ratio (TOFR) of <0.7. However, subsequent studies have discovered that residual neuromuscular blockade can occur at TOFR \geq 0.9, as per the review by Murphy and Brull in 2010.¹¹ These authors concluded that, "Residual neuromuscular block is an important patient safety issue and that neuromuscular management affects postoperative outcome."¹¹

Reversal of NMB

Acetylcholinesterase inhibitors, such as neostigmine, are commonly used to reverse NMB at the conclusion of surgery; however, they may have unwanted side-effects such as tachycardia, nausea, confusion, constipation, and dry mouth.¹² More importantly, when used without appropriate nerve stimulator monitoring and dosing, they may actually increase NMB by creating very high concentrations of acetylcholine at the neuromuscular junction, which can have an antagonistic effect.¹³

There are surprisingly few publications of adequate sample size examining the effect of NMB with and without a reversing agent on substantive outcomes important to the patient. Two of the largest studies examining this issue had significant limitations with respect to propensity matching for patient co-morbidities and/or for administration of neostigmine. These issues limit the clarity of the associations between poor outcomes and the use of NMB agents, reversal, inadequate monitoring, and inadequate reversal. These relationships are difficult to study in a retrospective manner with incomplete datasets and variable practice patterns and are better examined in large prospective studies.^{14,15} While some providers may believe that near complete spontaneous recovery does occur by the end of a surgical procedure without the use of NMB reversal agents, a variety of studies contradict this notion. One most notable large clinical trial by Debaene and colleagues in more than 500 patients suggested that 45% of patients examined after a single dose of an intermediate acting NMB (without a NM reversal agent) had a TOFR <0.9 in PACU.¹⁶ In addition, even 2 hours after administration of a single intermediate acting NMB, the TOFR was <0.7 in 10% of patients and <0.9 in 37% of the patients studied. Therefore, cautious titration of NMB reversal by using NM monitoring may reduce the risk of residual neuromuscular blockade.

Current Practice

Naguib and colleagues conducted an internet survey of active members of the Anesthesia Patient Safety Foundation and the European Society of Anaesthesiologists in 2008; 2,636 completed surveys were received.¹⁷ We did not find a more recent survey of U.S. anesthesiologists. The majority of both U.S. and European respondents estimated the incidence of clinically significant postoperative residual neuromuscular weakness to be <1%. Routine pharmacologic reversal was reported by 18% of respondents in Europe and 34% in the U.S.

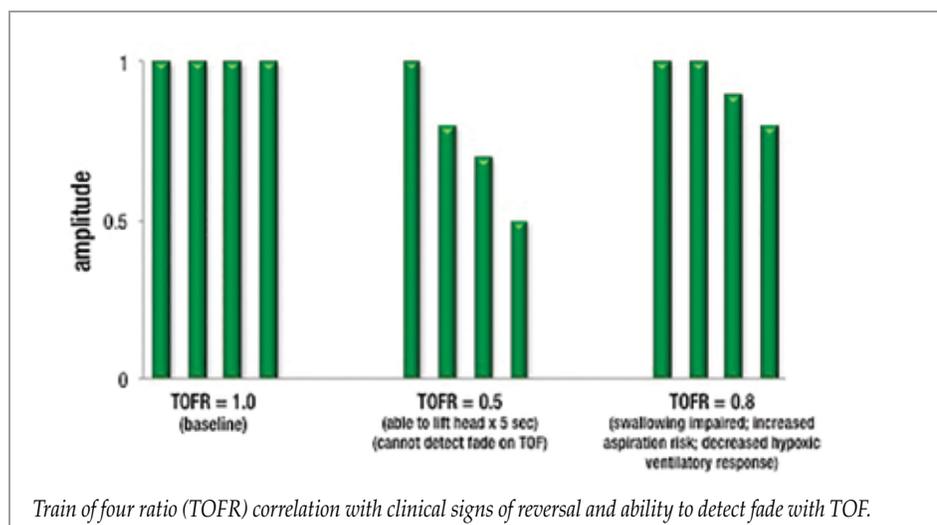
Conclusions

There is a consensus in the recent literature that residual neuromuscular blockade is common and is associated with an increased risk of adverse outcomes, particularly respiratory. It is also clear that the use of NMB monitoring and appropriate reversal with neostigmine is highly variable among anesthesia providers and is thought to be primarily responsible for the high incidence of residual NMB in the recovery room.

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Reversal of NMB Highly Variable Among Anesthesia Providers

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References

- Carman JA. History of curare. *Anaesthesia* 1968;23:706–707.
- Ibanez FM. Three enigmas in the history of curare before Sir Walter Raleigh. *Int Rec Med Gen Pract Clin* 1951; 164:700–710.
- West R. Curare in man. *Proc R Soc Med* 1932;25:1107–1116.
- Bennett AE. Preventing traumatic complications in convulsive shock therapy by curare. *J Am Med Assoc* 1940;114:322–324.
- Griffith HR. The use of curare in general anesthesia. *Anesthesiol* 1942;3:418–420.
- Beecher HK, Todd DP. A study of the deaths associated with anesthesia and surgery: based on a study of 599, 548 anesthetics in ten institutions 1948–1952, inclusive. *Annals of Surgery* 1954;140:2–35.
- Saklad M. Grading of patients for surgery. *Anesthesiol* 1941; 2:281–284.
- Viby-Mogensen J, Jorgensen BC, Ording H. Residual curarization in the recovery room. *Anesthesiol* 1979;50:539–541.
- Plaud B, Debaene B, Donati F et al. Residual paralysis after emergence from anesthesia. *Anesthesiol* 2010;112:1013–1022.
- Donati F. Residual paralysis: a real problem or did we invent a new disease? *Canadian Journal of Anesthesiology* 2013;60:714–19.
- Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg* 2010;111:120–128.
- Abad-Gurumeta A, Ripolles-Melchor J, Casans-Frances R et al. A systematic review of sugammadex vs neostigmine for reversal of neuromuscular blockade. *Anaesthesia* 2015;70:1441–1452.
- Goldhill DR, Wainwright AP, Stuart CS, Flynn PJ. Neostigmine after spontaneous recovery from neuromuscular blockade. Effect on depth of blockade monitored with train-of-four and tetanic stimuli. *Anaesthesia* 1989;44:293–9.
- Arbous MS, Meursing AE, Van Kleef JW et al. Impact of anesthesia management characteristics on severe morbidity and mortality. *Anesthesiol* 2005;102:257–268.
- Grosse-Sundrup M, Henneman JP, Sandberg WS et al. Intermediate acting non-depolarizing neuromuscular blocking agents and risk of postoperative respiratory complications: prospective propensity score matched cohort study. *BMJ* 2012; 345:e6329.
- Debaene B, Plaud B, Dilly MP, Donati F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *Anesthesiology* 2003;98:1042–8.
- Naguib M, Kopman AF, Lien CA et al. A survey of current management of neuromuscular block in the United States and Europe. *Anesth Analg* 2010;111:110–119.

Letter to the Editor:

The Structure and Process of PACU Handoff—How to Implement a Multidisciplinary PACU Handoff Checklist

To the Editor:

We would like to thank Tan and colleagues for their response to our study, “Improving Post Anesthesia Care Unit (PACU) Handoff by Implementing a Succinct Checklist.”^{1,2} They address many of the important challenges in standardization of healthcare processes and we are happy to continue the discussion. This topic is of growing concern among anesthesia providers as evidenced by several studies published in the past year that have examined the benefit of a standardized handoff.^{3,4} Tan and colleagues bring up two important topics that we would like to emphasize in this letter: the *structure* and *process* of PACU handoff.

At their institution, Tan and colleagues found that: “following a rigid checklist may elicit resistance among more experienced clinicians because it interferes with the ‘flow’ of their practiced, yet not necessarily complete, handoff reports.” A less-structured handoff/checklist may appeal to experienced clinicians; however, at Medstar Georgetown University Hospital (MGUH), the majority of PACU handoffs are completed by trainees (residents and student nurse anesthetists). Patient handoff is a clinical skill that we expect all of our trainees to master. Reinforcing this structured format of PACU handoff establishes a culture of patient safety that will continue as our trainees graduate into practice. Our experienced clinicians may adopt a similar handoff structure described by Tan and colleagues with a verbal “story” preceding a “Read and Verify” review of the checklist, although a structured reading of the

checklist is encouraged. Even the most experienced clinicians are at times distracted or leave out important information.

We agree with another point emphasized by Tan and colleagues—it is not sufficient to address the content of PACU handoffs, we must also address the process. We are now engaged in a PACU handoff initiative that includes our surgical colleagues. This multidisciplinary PACU handoff will bring all parties to the (bedside) table to ensure complete, efficient handoff of care in the PACU. Our multidisciplinary handoff allows for a structured handoff, starting with “Patient Admission and Assessment,” where each of the three handoff teams engages in specific activities to ensure a quick, efficient admission to the PACU. This first step addresses patient safety and stability prior to focusing on face-to-face handoff.

We are encouraged that Tan and colleagues include a surgical handoff on their checklist and we wonder whether it is included in a structured handoff effort or whether the two handoffs exist independently. At MGUH, one of the keys to success in an organized multidisciplinary handoff effort is the support we have received from PACU nursing as well as both anesthesia and general surgery departments. The appointment of “local champions” has been cited as an important ingredient to success in previous successful checklist endeavors.⁵ We feel that strong support, from both the resident leaders and department faculty, has been integral in our overall success.

We would like to thank Tan and colleagues for providing their thoughtful feedback. We welcome continued discussion as we improve the exchange of information during the crucial moments of PACU handoff.

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References

- Tan J, Bhavsar S, Hagan K, Lasala J. An alternative succinct checklist offered for PACU handoff communication. *APSF Newsletter* 2015; 30(2):37–38.
- Potestio C, Mottla J, Kelley E, DeGroot K. Improving post anesthesia care unit (PACU) handoff by implementing a succinct checklist. *APSF Newsletter* 2015;30:13–15.
- Weinger MB, Slagle JM, Kuntz AH, Schildcrout JS, Banerjee A, Mercado ND, Bills JL, Wallston KA, Speroff T, Patterson ES, France DJ. A multimodal intervention improves post-anesthesia care unit handovers. *Anesthesia and Analgesia* 2015;121:957–971.
- Caruso TJ, Marquez JL, Wu DS, Shaffer JA, Balise RR, Groom M, Leong K, Mariano K, Honkanen A, Sharek PJ. Implementation of a standardized postanesthesia care handoff increases information transfer without increasing handoff duration. *Joint Commission Journal on Quality and Patient Safety* 2015;41:35–42.
- Conley DM, Singer SJ, Edmondson L, Berry WR, Gawande AA. Effective surgical safety checklist implementation. *Journal of the American College of Surgeons* 2011;212:873–879.