Consensus Statement on Perioperative Use of Neuromuscular Monitoring

Mohamed Naguib, MB BCh, MSc, FCARCSI, MD,* Sorin J. Brull, MD, FCARCSI (Hon),† Aaron F. Kopman, MD,‡ Jennifer M. Hunter, MBE, MB ChB, PhD, FRCA, FCARCSI (Hon),§ Béla Fülesdi, MD, PhD, DSci,|| Hal R. Arkes, BA, PhD,¶ Arthur Elstein, PhD,# Michael M. Todd, MD,** and Ken B. Johnson, MD††

A panel of clinician scientists with expertise in neuromuscular blockade (NMB) monitoring was convened with a charge to prepare a consensus statement on indications for and proper use of such monitors. The aims of this article are to: (a) provide the rationale and scientific basis for the use of quantitative NMB monitoring; (b) offer a set of recommendations for quantitative NMB monitoring standards; (c) specify educational goals; and (d) propose training recommendations to ensure proper neuromuscular monitoring and management. The panel believes that whenever a neuromuscular blocker is administered, neuromuscular function must be monitored by observing the evoked muscular response to peripheral nerve stimulation. Ideally, this should be done at the hand muscles (not the facial muscles) with a quantitative (objective) monitor. Objective monitoring (documentation of train-of-four ratio ≥0.90) is the only method of assuring that satisfactory recovery of neuromuscular function has taken place. The panel also recommends that subjective evaluation of the responses to train-of-four stimulation (when using a peripheral nerve stimulator) or clinical tests of recovery from NMB (such as the 5-second head lift) should be abandoned in favor of objective monitoring. During an interim period for establishing these recommendations, if only a peripheral nerve stimulator is available, its use should be mandatory in any patient receiving a neuromuscular blocking drug. The panel acknowledges that publishing this statement per se will not result in its spontaneous acceptance, adherence to its recommendations, or change in routine practice. Implementation of objective monitoring will likely require professional societies and anesthesia department leadership to champion its use to change anesthesia practitioner behavior. (Anesth Analg 2017;XXX:00-00)

I have been impressed with the urgency of doing. Knowing is not enough, we must apply. Being willing is not enough; we must do.

Leonardo di ser Piero da Vinci (1452-1519)

he panel recommendations are intended for anesthesia care providers who use neuromuscular blocking drugs (NMBDs) and reversal agents and for professional organizations that develop practice advisories and guidelines regarding minimum standards for patient monitoring of neuromuscular blockade (NMB).

From the *Department of General Anesthesia, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland Clinic, Cleveland, Ohio; †Department of Anesthesiology, Mayo Clinic College of Medicine, Jacksonville, Florida; ‡Department of Anesthesiology, Weill Cornell Medical College, New York, New York; \$Department of Musculoskeletal Biology, University of Liverpool, Liverpool, United Kingdom; ||Faculty of Medicine, Department of Anesthesiology and Intensive Care, University of Debrecen, Debrecen, Hungary; ¶Department of Psychology, The Ohio State University, Columbus, Ohio; #Department of Medical Education, University of Illinois, College of Medicine at Chicago, Chicago, Illinois; *Department of Anesthesiology, University of Minnesota Medical School, Minneapolis, Minnesota; and ††Department of Anesthesiology, University of Utah, Salt Lake City, Utah.

Accepted for publication October 10, 2017.

Funding: None.

Conflicts of Interest: See Disclosures at the end of the article.

Reprints will not be available from the authors.

Address correspondence to Mohamed Naguib, MB BCh, MSc, FCARCSI, MD, Department of General Anesthesia, Anesthesiology Institute, Cleveland Clinic, 9500 Euclid Ave, NB3-78, Cleveland, OH 44195. Address e-mail to naguibm@ccf.org.

Copyright © 2017 International Anesthesia Research Society DOI: 10.1213/ANE.000000000002670

RECOMMENDATIONS

- Quantitative (objective) NMB monitoring should be used whenever a nondepolarizing NMBD is administered:
 - a. Quantitative monitoring is defined as an objective real-time measurement of the train-of-four ratio (TOFR). The difference between quantitative and qualitative assessments of NMB is in their ability to objectively measure the TOFR. Qualitative (subjective) assessments using peripheral nerve stimulator (PNS) devices depend on the anesthesia practitioner estimating the strength of muscle contractions in response to train-of-four (TOF) stimulation by visual or tactile means only, and thus are prone to error.
 - b. The panel recognizes that replacing conventional PNS devices with quantitative monitoring equipment will take time and education. During this interim period, the use of a PNS in any patient receiving a NMBD is mandatory.
- 2. Subjective or clinical tests of NMB are not predictive of adequate neuromuscular recovery and are not sensitive to the presence of residual neuromuscular weakness; their use should be abandoned in favor of objective monitoring:
 - After the TOFR recovers to >0.40, clinicians can no longer detect the presence of fade by tactile or visual observation (subjectively). Therefore, clinicians may assume complete recovery from NMB

- (ie, TOFR ≥0.9) despite the actual presence of minimal or shallow degrees of NMB (Table 1).
- b. After emergence from anesthesia and tracheal extubation, undetected minimal or shallow levels of NMB (Table 1) can lead to adverse airway or pulmonary complications.
- c. Clinical signs (such as the 5-second head lift or sustained handgrip) and clinical tests (such as presence of spontaneous respiration) do not guarantee complete resolution of NMB and no longer have a place as the sole determinant of adequate recovery of neuromuscular function (Table 2).
- Professional organizations should develop practice standards and guidelines detailing how best to monitor and manage perioperative administration of NMBDs.
- 4. Terms that describe the levels of NMB should be standardized. This consensus statement provides proposed definitions of complete, deep, moderate, shallow, and minimal NMB based on quantitative NMB monitoring criteria (Table 1).

INTRODUCTION

The impetus for developing this consensus statement was based on a series of reports that indicate a low frequency of routine neuromuscular monitoring $^{5-8}$ and a lack of anesthesia practitioner awareness of the high incidence (40%–60%) of residual NMB 9,10 and its associated morbidity. $^{2,3,11-15}$

Potentially unsafe practices in managing perioperative NMB persist. The use of PNS devices for managing NMB is unreliable when interpreting the subjective evoked responses by visual or tactile means and does not allow clinicians to consistently detect residual NMB (Table 1). 16,17

There is also poor awareness of the inability of clinical signs and tests (eg, 5-second head lift, grip strength, or tidal volume) to detect modest levels of residual NMB.^{5,18,19} For example, at a TOFR <0.7 (which does not represent adequate recovery), >70% of patients can sustain a head lift for 5 seconds.^{17–19} The use of clinical signs of recovery as well as subjective evaluations of the TOFR to assess the levels of NMB should be abandoned ultimately.^{1,3,4,20–23} The panel recognizes that translation of research findings into clinical practice can take up to 17 years,^{24,25} but aims

to shorten the transition from PNS devices to routine use of objective NMB monitors through widespread education and training, while realizing that ultimately only the introduction of clinical guidelines is likely to change routine anesthesia practice.

The main recommendations of this document are that quantitative monitoring should be used to guide the intraoperative use of NMBDs. Given the wide variability of patient response to these drugs, ^{26–28} such practice will help to ensure effective antagonism and reliably prevent residual neuromuscular weakness and its attendant complications. ²⁰ Implementation of departmental educational programs that enforce the use of objective monitoring clearly demonstrated a reduction in the incidence of postoperative NMB (from 62% to <4%)²⁹ and the need for NMBD-related reintubations in postanesthesia care unit (PACU). ^{20,30}

A brief review of the most recent literature indicates that in some countries, even PNS devices are often unavailable in teaching institutions.5,6 In countries where both PNS devices and objective monitors are available, 50% of clinicians only use clinical tests, and only 11% of the clinicians who use "some monitoring" routinely use an objective monitor.31 Only 17% of clinicians monitor neuromuscular function "often" (defined as "almost daily"), while 83% use no monitoring or use subjective criteria.8 Possible reasons for the apathy in the use of neuromuscular objective monitors may include lack of concern for the clinical significance of residual neuromuscular block or lack of suitable neuromuscular monitors.^{5,8} Although most clinicians appear to recommend that a neuromuscular function monitor be available in every operating room, less than half would recommend a quantitative monitor, apparently being satisfied with subjective assessment or with the equally unreliable clinical testing. This position is difficult to understand, given that the capital expenditure required to acquire objective monitoring equipment is relatively small, and the cost of disposable electrodes is low.8

NEUROMUSCULAR MONITORING

Despite an editorial consensus that monitoring of neuromuscular function should be mandatory whenever a nondepolarizing NMBD is administered, ^{21,22,32–36} this standard is far from being implemented universally. Throughout this

Table 1. Levels of Neuromuscular Block			
Level of Block	Depth of Block	Objective Measurement (Quantitative Monitor) at the Adductor Pollicis Muscle	Subjective Evaluation (PNS) at the Adductor Pollicis Muscle ^a
Level 5	Complete block	PTC = 0	PTC = 0
Level 4	Deep block	$PTC \ge 1$, $TOFC = 0$	$PTC \ge 1$, $TOFC = 0$
Level 3	Moderate block	TOFC = 1-3	TOFC = 1-3
Level 2b	Shallow block	TOFR < 0.4	TOFC = 4; TOF fade is present
Level 2a	Minimal block	TOFR = 0.4-0.9	TOFC = 4; TOF fade is not detectable
Level 1	Acceptable recovery	TOFR ≥ 0.9	Cannot be determined

Level 2a: This level of block encompasses a wide spectrum of signs and symptoms. At TOF of 0.40, vital capacity is reduced by 26% (8%–41%) and handgrip by 80%. A TOFR in the range of 0.60–0.80 is associated with significant impairment of the swallowing mechanism and the potential for pulmonary aspiration of gastric contents. At a TOFR of 0.70, grip strength is reduced by >40%, and jaw apposition is often impossible (inability to retain a tongue depressor between incisor teeth). After the TOFR exceeds 0.85, only very mild symptoms of residual weakness should be anticipated, although diplopia and subjective weakness may persist for several hours.

Abbreviations: NMB, neuromuscular blockade; PNC, peripheral nerve stimulator; PTC, posttetanic count; TOF, train of four; TOFC, train-of-four count; TOFR, train-of-four ratio.

^aSubjective evaluation of NMB is not recommended, but it is included as an interim transition from current practice to the preferred, objective monitoring-based practice.

Table 2. Quantitative and Qualitative Evaluations of **Neuromuscular Function**

Quantitative (Objective) **Evaluation**

analyzes, and displays the TOFR in real time.

Qualitative (Subjective) Evaluation

device that measures, the strength of muscle contractions in response to TOF stimulation by visual or tactile means using a PNS-or Clinicians infer adequate return of neuromuscular function from clinical signs, such as 5-s head lift, tidal volume, grip strength.

Abbreviations: PNC, peripheral nerve stimulator; TOF, train of four; TOFR, train-of-four ratio.

consensus statement, the term "monitor" will be restricted to those devices that measure, analyze, and display the TOFR in real time (Table 1). These quantitative monitors provide an objective measure of the TOFR.

A monitor must be differentiated from a PNS, which only provides nerve stimulation without measuring the evoked muscular response. These units should be referred to as "qualitative devices." The anesthesiologist is the monitor who makes a subjective evaluation of the strength of the muscle response.

Perioperative neuromuscular monitoring has multiple benefits: on induction of anesthesia, absence of a TOF response (train-of-four count [TOFC] = 0) signals readiness for laryngoscopy and tracheal intubation, improves intubating conditions, and reduces the incidence of vocal cord damage.³⁷ Intraoperative monitoring abets optimal surgical conditions, guides appropriate NMBD dosing, and signals readiness for pharmacologic antagonism.

Achievement of a TOFR ≥0.90 indicates recovery from NMB sufficient for tracheal extubation. NMB monitoring has been shown to decrease the incidence of residual neuromuscular block and to reduce the incidence of postoperative airway and respiratory complications. 11,20 It is estimated that as many as 112,000 patients annually in the United States are at risk of adverse respiratory events associated with undetected NMB.32 The avoidance of postoperative pulmonary complications such as persistent atelectasis and aspiration pneumonitis among others is particularly important, since 14%-30% of patients who develop them die within 30 days of major surgery.³⁸ Morbidity is also increased in patients who develop postoperative pulmonary complications; their length of hospital stay is prolonged by up to 17 days.³⁸ Health care costs are increased by such complications by >\$25,000 per hospital admission.39

Neuromuscular Blockade

There is no general consensus for the meaning of terms such as "deep" or "moderate" neuromuscular block. Recommended definitions for levels of NMB are presented in Table 1.40,41 The 2 most superficial levels of block are of particular interest as they cannot be detected by subjective (tactile or visual) observation. They require objective measurement.

The current standard for "adequate recovery" from neuromuscular block is the return of the TOFR to ≥0.9 measured at the adductor pollicis muscle.

Neuromuscular Stimulation Patterns

- 1. Single twitch stimulation: Single twitch represents the evoked response to an individual stimulus at a frequency of 0.1 or 0.15 Hz (1 twitch every 10 or 6.7 seconds, respectively). This stimulation pattern per se has no clinical utility and is primarily used for determining the potency (dose response) of NMBDs.
- 2. TOF stimulation: TOF stimulation is composed of four stimuli separated by 0.5 second (a frequency of 2 Hz) and is usually repeated every 10-20 seconds.42-44 The TOFR is calculated by dividing the amplitude of the fourth response (T4) by the amplitude of the first response (T1); T4/T1, or the TOFR. TOF is the most appropriate mode of neuromuscular assessment in clinical practice, and the determination of the TOFR requires the use of a quantitative monitoring device (Table 1).
- 3. Tetanic stimulation and post-tetanic twitch count (PTC): A unique feature of nondepolarizing block is that after a tetanic stimulus, there is a brief augmentation of the mechanical response. This phenomenon is termed post-tetanic facilitation or potentiation. This attribute is helpful in determining the depth of block when the TOFC is 0. PTC is evaluated by counting the number of muscle responses when a sequence of 20 stimulations at 1 Hz is delivered 3 seconds after a 5-second, 50-Hz tetanus.⁴⁵ Tetanic stimuli of higher frequencies (100-200 Hz) are unphysiologic as they can induce fade even in the absence of NMBDs and should not be used clinically.46-48 Tetanic stimulation results in acceleration of twitch recovery at the stimulated muscle. This may have clinical implications, in that tetanic stimulation "... may lead to unnecessary repeated administration of neuromuscular blocking agents, or at the other extreme, to false estimation that adequate neuromuscular function exists."49 Therefore, tetanic stimulation should not be repeated more frequently than every 2-3 minutes.⁴⁹ TOF stimulation, unlike tetanic stimulation, does not potentiate subsequent neuromuscular responses after its application, as long as the interval between successive trains is >12 seconds.⁵⁰ The PTC is used to monitor the depth of neuromuscular block when deep block is required, as in open-globe ophthalmic or certain intracranial operations.^{51,52} There is never an indication for maintaining a PTC of <1 or 2.

For a detailed discussion of the various neurostimulation patterns used in the clinical setting, see the recent review by Naguib et al.41

Monitoring Sites

Historically, the vast bulk of the early research on the actions of NMBDs was performed on the ulnar nerve adductor pollicis motor unit using mechanomyography (MMG). This unit became the gold standard by which we measure the clinical effects of NMBDs. The ulnar nerve also innervates the abductor digiti quinti and first dorsal interosseous muscles. These muscles have similar responses to the adductor pollicis, and their responses are usually measured with electromyographic (EMG) monitors. Electrical activation of peripheral motor nerves requires 2 electrodes to produce a current flow. The depolarizing (negative) electrode is placed distally 1 cm proximal to the wrist crease on the radial side of flexor carpi ulnaris, while the other (positive) electrode is placed proximally on the volar forearm. ^{53,54} The distance between the 2 electrodes should not exceed 5 cm. This orientation ensures maximal neuronal stimulation and muscular response. ⁵³

If the hand is not accessible for monitoring, stimulation of the facial nerve may be used. However, facial muscles such as the orbicularis oculi and corrugator supercilii are more resistant to the actions of nondepolarizing blockers, and their time course (onset and recovery) may differ from responses at the hand muscles.55,56 Thus, a TOFC of 4 at the face may be accompanied only by a TOFC of 1 or no response at the hand. 57,58 The electrodes should be placed near the stylomastoid foramen (just below and anterior to the mastoid bone) or just anterior to the ear lobe to evoke contraction of the orbicularis oculi or the corrugator supercilii muscles. The evoked response is usually estimated subjectively (not recommended), but can be quantified using an acceleromyographic (AMG) transducer. However, even AMG responses may be suspect, as the amplitude of the evoked response is usually weak. Facial nerve stimulation should not be used to assess adequacy of reversal because of the difference in sensitivities between hand and facial muscles. The stimulator electrodes must be moved to the ulnar nerve at the end of the surgical procedure to ensure adequate recovery of neuromuscular function at the adductor pollicis muscle before tracheal extubation.

QUANTITATIVE (OBJECTIVE) NEUROMUSCULAR MONITORS

NMBDs have no effect on muscle contractility nor on muscle membrane excitability. However, direct muscle stimulation can result in an evoked response even when the level of drug-induced paralysis is profound; this is often the case when monitoring facial muscles.

Mechanomyography

The majority of the early research on neuromuscular function was performed by measuring the mechanical response with a force transducer to indirect muscle stimulation.⁵⁹ MMG measures isometric muscle contraction (usually the adductor pollicis muscle) in response to ulnar nerve stimulation. Despite its precision and repeatability, MMG has several limitations: it requires bulky equipment, unencumbered access to the monitored hand, application and maintenance of pretension (preload) of 200-300 g, and an elaborate setup that requires a fixed arm position throughout the surgical procedure to retain baseline calibration. While MMG recordings are considered a "gold standard" for accuracy, no MMG device is commercially available for routine clinical use in the operating room, and because of technical considerations, it is doubtful that this situation will change.

Electromyography

An alternative gold standard to MMG is EMG. EMG measures the peak-to-peak amplitude or the integrated area under the waveform curve of the evoked muscle action

potential to measure the intensity of the evoked response. The agreement between EMG recordings and other methods of monitoring neuromuscular function has been studied extensively.60-62 While evoked EMG and MMG responses do show minor dissimilarities, the 2 can be used interchangeably. In theory, measuring the electrical response of muscle (EMG) rather than the mechanical response (MMG) as a barometer of neuromuscular transmission has advantages. The EMG is not affected by changes in muscle contractility; immobilization of the muscle to be studied is not essential, and no preload is needed; restricted motion of the thumb (eg, when the patient's arms are tucked at the sides) does not prevent EMG neuromuscular monitoring; and sites other than the hand are more easily monitored, if the arms are not available. In addition, the EMG response is less dependent on maintenance of intraoperative normothermia than mechanical techniques. 63,64

At present, there are no commercially available free-standing, battery-operated EMG monitors, although members of the panel are aware of several companies that have expressed an interest in developing one. At least 1 manufacturer (eg, GE Healthcare, Chicago, IL) has an EMG module that can be included in their integrated patient monitoring systems (ElectroSensor NMT Module).

Acceleromyography

This approach to neuromuscular monitoring is based on Newton's second law of motion (force = mass × acceleration). Since the mass of the thumb remains constant, acceleration is directly proportional to force. For measurement of acceleration, a piezo-electric ceramic wafer is fixed to the thumb. When the thumb moves as a result of ulnar nerve stimulation, an electrical signal is produced in the piezo-electric crystal that is proportional to the thumb acceleration. This signal can be digitized, processed, and electronically displayed in real time. ^{65,66}

Raw AMG data have an idiosyncrasy. In contrast to MMG and EMG where the control (baseline) TOFR approximates 1.00 (100%), the control AMG-measured TOFR is more likely to be >1.00 (>100%). Values between 1.10 (110%) and 1.20 (120%) are common, and values of 1.40 (140%) are not rare. Thus, if the baseline TOFR is 1.47 (147%), postoperative return of the displayed TOFR to a value of 0.90 (90%) would correspond to an actual TOFR of only 0.61 (61%) (0.9 \div 1.47 = 0.61). If it is known that the AMG device being used displays raw TOFR data, such a mathematical correction (normalization) needs to be applied. Therefore, when using AMG, a more precise definition of acceptable recovery of NMB would be return of TOFR to 90% of the baseline TOF value

To simplify routine clinical use, several AMG manufacturers do not allow their units to display TOFRs >1.00 (100%). This may give clinicians erroneous information regarding the acceptable level of recovery. Unfortunately, the algorithms many units employ in converting raw to displayed values are often not shared with the user. AMG monitors may be difficult or impossible to use clinically when the free movement of the thumb cannot be assured. The TOF-Watch is no longer commercially available worldwide. Several new hand-held AMG monitors have been recently introduced which employ triaxial or 3-dimensional

technology to make their transducers less dependent on correct alignment of the piezoelectric wafer with the direction of thumb movement. However, most of the AMG units on the market have not been validated against an EMG or MMG gold standard device.

Kinemyography

An alternate approach to the use of a piezoelectric motion sensor was developed, wherein "deformation of a piezoelectric substance causes a redistribution of charge in the material which leads directly to electron flow to balance the charge."68 The electron flow produces a voltage that is measured by electrodes placed across the piezo material. The charge is rapidly dissipated owing to internal resistance; thus, only dynamic changes can be measured when using these devices. 68 Sensor output occurs when the piezo material film spans a movable joint and muscle movement from evoked stimulation bends the piezoelectric film, which generates a voltage proportional to the amount of bending. To distinguish this technology from AMG, it is referred to as kinemyography (KMG). There is at least one manufacturer that currently markets a monitor employing this technology (GE Healthcare MechanoSensor-NMT Module, GE Healthcare). KMG gives measurements that are repeatable and provides reasonable correlation with a force transducer. Thus, they can be used clinically to assess recovery from neuromuscular block. However, the wide limits of agreement of KMG with MMG and EMG rule out research applications.⁶⁹ As with AMG monitors, KMG monitors cannot be used clinically when the thumb movement is restricted.

LIMITATIONS OF NEUROMUSCULAR MONITORING

Despite the relatively low cost of neuromuscular monitors, particularly when considering the economic costs associated with complications that result from unmonitored care, the acceptance of neuromuscular devices in clinical practice remains poor. A recent survey of the most common difficulties experienced during objective monitoring (using AMG in 91% of cases) included perceived error messages on the monitor (27% of respondents), fluctuating TOF values (41%), position of the patients' arm (16%), and calibration problems including differences between visual and objective measurements (6%).70 A major limitation to wide spread adoption of objective neuromuscular monitors is not their cost, but their ease of use. New monitors that will not be affected by patient hand positioning, that are selfcalibrating, that are reliable, that are easy to set up, and that produce repeatable responses are needed.

CURRENT CONSENSUS STATEMENTS REGARDING THE USE OF NMB MONITORING

Over the last 2 decades, recommendations on the use of NMB monitors have been published by several professional societies and organizations throughout the world. For the most part, these consensus statements endorse the use of quantitative monitoring in place of clinical signs or subjective assessments of TOF fade. For example, in 2000, the French published recommendations regarding the "management of incomplete reversal of neuromuscular blockade." This document states that "clinical assessment cannot guarantee the absence of residual blockade; instrumental

monitoring is the main means for assessment of reversal of NMB. It is based on the TOF stimulation at adductor pollicis, with visual or tactile evaluation of the evoked response. The presence of 4 responses to the TOF stimulation is not a sufficient criterion of full reversal of blockade. It must be confirmed by the absence of fade with double burst stimulation (DBS) or TOF recording."⁷¹

In 2010, the Board of the Czech Society of Anaesthesiology and Intensive Care Medicine published consensus-based practice parameters regarding NMB monitoring. They concluded that both clinical assessment and subjective evaluation of evoked responses are unreliable, and using a monitoring device "appears to be the most appropriate method at present time."

The Association of Anaesthetists of Great Britain and Ireland 2016 consensus document on the standards of monitoring during anesthesia and recovery72 states that "... an objective, quantitative peripheral nerve stimulator is the best way to monitor the degree of neuromuscular blockade" and "Ideally the adductor pollicis muscle response to ulnar nerve stimulation at the wrist should be monitored." This document also states "a peripheral nerve stimulator is mandatory for all patients receiving neuromuscular blockade drugs" and "a quantitative peripheral nerve stimulator is required to accurately assess the train of four ratio, but other stimulation modalities (eg double burst or post tetanic count) can also be used for assessment." The authors concluded that "anaesthetic departments are encouraged to replace existing qualitative nerve stimulators with quantitative devices."

As of the date this article was written, the American Society of Anesthesiologists (ASA) has remained silent on the need for monitoring of neuromuscular function in the perioperative period. The ASA Standards for Basic Anesthetic Monitoring (amended in 2010 and affirmed in 2015) makes no mention of the need for neuromuscular monitoring.⁷³ The reason for their reticence to address this issue is unclear.

How This Consensus Statement Differs From What Is Already Available

This consensus statement stresses 2 issues. First, the statement reiterates that visual and/or tactile (subjective) evaluation of evoked responses is unreliable. While subjective assessment may help clinicians assess complete block (when PTC = 0), deep block (when PTC \geq 1 and TOFC = 0), and moderate block (TOFC = 1-3; Table 1), readiness for tracheal extubation (TOFR ≥0.90) cannot be assured by subjective evaluation, as the absence of subjective fade does not consistently identify complete recovery. Quantitative monitoring is required to establish complete recovery. Second, the absence of fade to DBS to ensure adequate recovery from NMB is also unreliable. DBS (a mini-tetanic sequence of 3 stimuli at 50 Hz, followed 750 milliseconds later by another sequence of 2 or 3 stimuli at 50 Hz) fails to identify (by subjective means) the presence of NMB at a TOFR of ≥0.60.⁷⁴ The consensus of this panel is that these modalities are inadequate to differentiate shallow or minimal blockade from acceptable recovery and that unrecognized shallow or minimal blockade may lead to an unacceptable increase in the risk of perioperative critical respiratory events.

PRACTICAL HURDLES TO OVERCOME IN IMPLEMENTING RECOMMENDATIONS

Some authors have asked, "Why, with the growing volume and apparent quality of evidence and with the growing technological and organizational efficiency of indexing, storing, retrieving, synthesizing, and disseminating evidence, would practitioners ... seem to be having difficulty incorporating the evidence into their practices and using it more assiduously?"24 The gap between science and practice is due to multiple factors: on the one hand, clinicians may insist that their practice is best tailored for their patients and they do not need to change it regardless of novel scientific data. On the other hand, researchers are convinced that their data are so important and applicable to routine practice that publication of scientific results will be inevitably embraced and adopted by all practitioners. An additional barrier to acquiring and implementing new knowledge is not necessarily the understanding of new concepts, but rather the unlearning of old and outdated "knowledge." This unlearning process has been termed "deimplementation" or "deadoption," and physicians have a particularly difficult time unlearning outdated practices.⁷⁵ Much has been written in the past decade about evidence-based medicine, and its role in abandoning ineffective medical practices to both improve patient safety and contain health care costs.⁷⁶ But change in medical practices that are not evidence based (deimplementation) is time consuming, costly and biased. For instance, some physicians would consider changing their practice only if it were proven to be harmful.⁷⁶

Another major hurdle to the implementation of objective monitoring is the limited experience with this modality in the anesthesia community. Clinicians who have little exposure to objective monitors are often unaware of the subtle yet important differences between data obtained from quantitative monitors and the limited (and erroneous) information generated by subjective evaluation using PNS or clinical signs of recovery. Moreover, many of the consequences of inadequate reversal seem to be either readily correctable in the PACU (with supplemental oxygen, airway manipulation/jaw thrust, or nasal airway) or occur after the clinician has left the patient's bedside to return to the operating room. Lack of monitoring expertise and inadequate assessment of neuromuscular function at the time of transfer of care to the PACU staff result in a belief that such monitoring is unnecessary. By contrast, clinicians with experience in quantitative monitoring recognize the wide variability in the duration of action of neuromuscular blocking agents, the exaggerated responses that can occur to even small doses of such drugs, the slow and incomplete reversal after "normal" doses of neostigmine or sugammadex, and the immediate difficulties encountered by the elderly, the obese, or respiratorycompromised patients.

Moreover, currently available devices are less than ideal. In addition to the limitations of AMG monitors, the majority of the quantitative monitors currently marketed may be difficult or impossible to use when the hand is not easily accessible. If for technical reasons (eg, positioning) these devices cannot be employed in a significant percentage of a clinician's patients, it is unlikely that the monitor will be ever viewed as essential to daily practice. It is the view of

this panel that the ideal quantitative monitor should be an EMG device. If integrated into a patient monitoring system, data output (TOFR and counts, PTCs, and perhaps EMG waveforms) should be retrievable from the anesthesia department's electronic record keeping system. However, a free-standing, battery operated, portable device would also be welcomed by those practices that do not have the ability to integrate NMT modules into their anesthesia workstations.

EDUCATION AND TRAINING RECOMMENDATIONS

Detailed national society guidelines regarding neuromuscular monitoring, combined with improved monitoring technology, would represent a major step toward achieving the goal of "potentially eliminating residual paralysis." As with pulse oximetry, expired gas analysis, temperature monitoring, and other now-standard monitors, clinicians need to be convinced of the value of such monitors, not simply be told to use them.

This panel recommends implementation of an educational program for all anesthesia practitioners who use or may use NMBDs. An outline for education and training is listed in Table 3.

Suggested Approaches to Quality Improvement Using NMB Monitoring

The panel proposes the following steps for anesthesia care providers to consider to improve the quality of NMB monitoring at their institutional level. The first step is to characterize the incidence of residual NMB at their institutional level. To accomplish this assessment, anesthesia care providers should measure the TOFR using a quantitative monitor upon arrival to the PACU in 100 consecutive patients who have received a nondepolarizing NMBD and report their findings to their clinician group. The intent of this step is to characterize the incidence of residual NMB and to expose clinicians to the use of quantitative monitoring to detect shallow and minimal NMB.

The second step is for anesthesia group leadership to promote "buy-in" to the new monitoring regimen by convening an advisory group comprising representatives from all clinical stakeholders (anesthesiologists, certified nurse anesthetists, recovery room nurses, and surgeons who request NMB). The advisory group would be tasked with identifying NMB monitor implementation barriers and recommend solutions to overcome them. An obvious necessity would be for quantitative monitors to be made readily available in every operating room and their correct performance repeatedly checked by qualified personnel. The intent of this step is to ensure that the anesthesia group leadership understands that NMB monitoring is crucial for patient safety and to underscore the importance of providing recurring opportunities for education and training for members of their group. Anesthesia group leadership, combined with education and training opportunities, will be required to convince clinicians of the need for transition from PNS to NMB monitor. As was clearly shown by changes in 1 institution, implementation of neuromuscular monitoring requires a continual process of education, repeated surveys of practice, and frequent feedback to clinicians. 20,29,77

Table 3. Recommended Education, Training, and NMB Monitoring Equipment

Education learning objectives

Define the incidence of residual NMB and current utilization rates of PNS devices and quantitative monitors.

Differentiate between quantitative and qualitative monitoring with emphasis on inadequacies of PNS.

Understand that clinical findings of tests such as the 5-s head lift, tidal volume, hand grip, etc, are unreliable signs and no longer have a place in evaluation of neuromuscular function.

Describe the levels of NMB and findings from quantitative monitoring that define each level.

Demonstrate proper electrode placement (anode/cathode orientation and distance between electrodes).

Understand the clinical implications of monitoring site (ulnar versus facial nerve).

Describe NMBD and reversal agent pharmacology with emphasis on how interpatient variability impacts the duration of NMB.

Training

Training should be provided by anesthesia care providers experienced in using NMB monitoring to guide administration of NMBDs and their reversal agents. An experienced anesthesia care provider is one who has used an NMB monitor to manage NMBDs in at least 50 patients.

Training should be in situ at the point of care by an anesthesia care provider experienced in NMB monitoring. Trainees should use the device in the presence of an experienced anesthesia care provider until competent in interpreting and using TOFR data to guide NMBD administration and reversal. Competence is at the discretion of the trainer, but should include a mastery of the concepts presented in the education section of this table. The suggested minimum number of patients in which a trainee uses objective monitoring in the presence of an experienced individual is ten.³

Experienced individuals should remain available to troubleshoot the use of monitors (and respond immediately to the complaints of "it is not working").

Equipment recommendations

Quantitative monitors should be available at all anesthetizing sites where nondepolarizing NMBDs are administered.

Ensure quantitative monitors are checked for proper function and are maintained by qualified personnel at the recommended intervals of the device manufacturer.

EMG devices offer advantages over other categories of monitoring devices: immobilization of the muscle to be studied is not essential and no preload is needed; restricted motion of the thumb (eg, when patient's arms are tucked sides) does not prevent neuromuscular monitoring; and sites other than the hand are more easily monitored if the arms are not available.

Data from quantitative monitors should be integrated into electronic medical records.

Abbreviations: EMG, electromyography; NMB, neuromuscular blockade; NMBD, neuromuscular blocking drug; PNS, peripheral nerve stimulator; TOFR, train-of-four ratio.

The third step is to evaluate the impact of NMB monitoring once implemented. The panel recommends a "before-and-after" implementation design that measures important patient outcomes, such as incidence of residual NMB when patients enter the PACU and the incidence of adverse respiratory events during the first 24 hours after surgery. Outcome measures should be clearly defined a priori.

BENEFITS OF CONSENSUS STATEMENT IMPLEMENTATION

- 1. Changing clinical practice: Modern medical practice is based on the use of guidelines and protocols. Best practice protocols should be simple to distribute both electronically among colleagues and staff and in hard-copy format for display in operating suites and other sites where anesthesiologists provide clinical care. Trainees are more likely to adhere to clinical guidelines if they are incorporated early into their educational track and would mount less resistance to incorporating them into their own routine practice. The introduction of minimal mandatory monitoring guidelines for practice during general anesthesia >30 years ago has resulted in their routine use. Such mandatory guidelines no longer are questioned.⁷⁸
- 2. Benefits of neuromuscular monitoring: It is rational for objective monitoring to be included in the minimal requirements necessary during every general anesthetic when NMBDs are administered. If NMB is monitored perioperatively, and residual block is avoided in the postanesthetic care unit, there is evidence that length of stay in the recovery area is shortened.⁷⁹ There is also a reduced incidence

- of postoperative respiratory complications. 11,20,80 Avoidance of all such complications will shorten the length of hospital stay and the cost of hospital admission.
- 3. Lead by professional organizations: There is peerreviewed evidence that recommendations found in guidelines are accepted by the majority of recipients.81 It also has been demonstrated that to improve clinical effectiveness, routine mechanisms should be used to promote organizational change.82 In other words, the same approach should be used for every new change in practice. This direction should come from major professional organizations; this is as important as changing an individual's attitudes and beliefs.82 Introduction of guidelines for neuromuscular monitoring in this way would increase its use; once it is accepted and required by one organization or institution, others will likely follow, resulting in the establishment of "local standards of practice." It is essential that such change in practice be introduced and supported initially by large and respected professional organizations, which will lead the way to acceptance of such changes regionally, nationally, and internationally. Symposia and panel discussions should be organized at national meetings. Accreditation standards should be determined nationally by such organizations, which should require residency and fellowship training on perioperative neuromuscular monitoring.
- 4. Implementation: Implementation of this statement must be supported by directors of anesthesia services at individual institutions and by program directors of training programs. The individuals

and organizations able to effect such changes from an administrative and financial standpoint must be then responsible for improving anesthetic practice and patient outcome. This will prove easier in the workplace if clear and easily accessible guidelines are produced by those national and international organizations in authority to do so.

5. Education and audit: An ongoing educational program is essential for the establishment of a change in routine practice. Reinforcement of knowledge and understanding of a new routine must be led by administrative chairs of departments of anesthesiology. Plans to monitor and evaluate such changes in practice should also be instituted, which in turn will lead to improved patient care.83 Obstacles to change should be identified within an institution and removed whenever possible. Appropriate research studies, preferably multiinstitutional and comprising large data-based outcomes, should be developed to investigate the obstacles to change; these outcome data will need to be deidentified to obtain accurate information. Changes in practice can be considered as knowledge orientated and behavior orientated.84 Staff must be first educated in the evidence base for the introduction of neuromuscular monitoring. If appropriate, a multidisciplinary approach involving all staff members of the operating room involved with anesthesia care should be then taken to instigate such change. This will lead to better team practice.85 Changes will also make the department more easily accountable, change behavior patterns in general, and make practitioners more open to change in the future.

CONCLUSIONS AND RECOMMENDATIONS

The panel recommends that whenever a neuromuscular blocker is administered, neuromuscular function must be monitored by observing the evoked muscular response to peripheral nerve stimulation. Ideally this should be done at the hand muscles (not the facial muscles) with a quantitative (objective) monitor. Objective monitoring (and documentation of TOFR ≥0.90) is the only method of assuring satisfactory recovery of NMB and patient safety. If a quantitative monitor is not available, the interim option is qualitative evaluation employing a PNS. Qualitative evaluation with a PNS device has substantial limitations; the absence of subjective tactile or visual fade does not guarantee adequate clinical recovery, and its proper use still requires an educational program. Clinical tests such as the 5-second head lift, tidal volume assessment, hand grip strength, etc are unreliable signs and should no longer be used in evaluating the adequacy of neuromuscular function.

The panel acknowledges that publishing a consensus statement per se will not result in widespread acceptance, adherence to its recommendations, or change in routine practice. Making quantitative monitors available in operating rooms will not ensure their use.²⁰ Implementation of objective NMB monitoring will require professional societies and anesthesia department leadership to champion its use to overcome anesthesia practitioner resistance. Implementation strategies should include education and training.^{20,29}

The expectation of this panel is that successful implementation of these recommendations will improve patient safety, quality of care, and cost-effectiveness. In addition, it is the aim of this panel to encourage professional societies to develop clinical guidelines for perioperative neuromuscular monitoring. Finally, the panel endorses a short transition period from clinical use of PNS devices to objective NMB monitoring.

DISCLOSURES

Name: Mohamed Naguib, MB BCh, MSc, FCARCSI, MD.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Mohamed Naguib declares no conflicts of interest.

Name: Sorin J. Brull, MD, FCARCSI (Hon).

Contribution: This author helped write the manuscript.

Conflicts of Interest: Sorin J. Brull is a member of the Anesthesia Patient Safety Foundation (APSF) Board of Directors (Rochester, MN); has received research funding from Merck & Co., Inc. (Kenilworth, New Jersey; funds to Mayo Clinic); is a principal and shareholder in Senzime AB (publ; Uppsala, Sweden); and a member of the Scientific Advisory Boards for ClearLine MD (Woburn, MA), The Doctors Company (Napa, CA), and NMD Pharma (Aarhus, Denmark).

Name: Aaron F. Kopman, MD.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Aaron F. Kopman declares no conflicts of interest.

Name: Jennifer M. Hunter, MBE, MB ChB, PhD, FRCA, FCARCSI (Hon).

Contribution: This author helped write the manuscript.

Conflicts of Interest: Jennifer M. Hunter declares no conflicts of interest

Name: Béla Fülesdi, MD, PhD, DSci.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Béla Fülesdi declares no conflicts of interest.

Name: Hal R. Arkes, BA, PhD.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Hal R. Arkes declares no conflicts of interest. Name: Arthur Elstein, PhD.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Arthur Elstein declares no conflicts of interest. Name: Michael M. Todd, MD.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Michael M. Todd declares no conflicts of interest.

Name: Ken B. Johnson, MD.

Contribution: This author helped write the manuscript.

Conflicts of Interest: Ken B. Johnson declares no conflicts of interest.

This manuscript was handled by: Jean-Francois Pittet, MD.

REFERENCES

- Heier T, Caldwell JE, Feiner JR, Liu L, Ward T, Wright PM. Relationship between normalized adductor pollicis train-offour ratio and manifestations of residual neuromuscular block: a study using acceleromyography during near steady-state concentrations of mivacurium. *Anesthesiology*. 2010;113:825–832.
- Eriksson LI, Sundman E, Olsson R, et al. Functional assessment of the pharynx at rest and during swallowing in partially paralyzed humans: simultaneous videomanometry and mechanomyography of awake human volunteers. *Anesthesiology*. 1997;87:1035–1043.
- Sundman E, Witt H, Olsson R, Ekberg O, Kuylenstierna R, Eriksson LI. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans: pharyngeal videoradiography and simultaneous manometry after atracurium. *Anesthesiology*. 2000;92:977–984.
- Kopman AF, Yee PS, Neuman GG. Relationship of the trainof-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *Anesthesiology*. 1997;86:765–771.

- Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ. A survey of current management of neuromuscular block in the United States and Europe. *Anesth Analg*. 2010;111:110–119.
- Videira RL, Vieira JE. What rules of thumb do clinicians use to decide whether to antagonize nondepolarizing neuromuscular blocking drugs? *Anesth Analg*. 2011;113:1192–1196.
- Kotake Y, Ochiai R, Suzuki T, et al. Reversal with sugammadex in the absence of monitoring did not preclude residual neuromuscular block. *Anesth Analg*. 2013;117:345–351.
- 8. Phillips S, Stewart PA, Bilgin AB. A survey of the management of neuromuscular blockade monitoring in Australia and New Zealand. *Anaesth Intensive Care*. 2013;41:374–379.
- Naguib M, Kopman AF, Ensor JE. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. Br J Anaesth. 2007;98:302–316.
- Fortier LP, McKeen D, Turner K, et al. The RECITE Study: a Canadian prospective, multicenter study of the incidence and severity of residual neuromuscular blockade. *Anesth Analg*. 2015;121:366–372.
- 11. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg*. 2008;107:130–137.
- Kumar GV, Nair AP, Murthy HS, Jalaja KR, Ramachandra K, Parameshwara G. Residual neuromuscular blockade affects postoperative pulmonary function. *Anesthesiology*. 2012;117:1234–1244.
- Arbous MS, Meursing AE, van Kleef JW, et al. Impact of anesthesia management characteristics on severe morbidity and mortality. *Anesthesiology*. 2005;102:257–268.
- 14. Bulka CM, Terekhov MA, Martin BJ, Dmochowski RR, Hayes RM, Ehrenfeld JM. Nondepolarizing neuromuscular blocking agents, reversal, and risk of postoperative pneumonia. *Anesthesiology*. 2016;125:647–655.
- Bronsert MR, Henderson WG, Monk TG, et al. Intermediateacting nondepolarizing neuromuscular blocking agents and risk of postoperative 30-day morbidity and mortality, and longterm survival. *Anesth Analg.* 2017;124:1476–1483.
- Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chraemmer-Jørgensen B. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology*. 1985;63:440–443.
- 17. Pedersen T, Viby-Mogensen J, Bang U, Olsen NV, Jensen E, Engboek J. Does perioperative tactile evaluation of the train-of-four response influence the frequency of postoperative residual neuromuscular blockade? *Anesthesiology*. 1990;73:835–839.
- 18. Beemer GH, Rozental P. Postoperative neuromuscular function. *Anaesth Intensive Care*. 1986;14:41–45.
- Cammu G, De Witte J, De Veylder J, et al. Postoperative residual paralysis in outpatients versus inpatients. *Anesth Analg*. 2006;102:426–429.
- Todd MM, Hindman BJ, King BJ. The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department. *Anesth Analg.* 2014;119:323–331.
- Brull SJ, Kopman AF. Current status of neuromuscular reversal and monitoring: challenges and opportunities. *Anesthesiology*. 2017;126:173–190.
- Naguib M, Johnson KB. Innovative disruption in the world of neuromuscular blockade: what is the "state of the art?" Anesthesiology. 2017;126:12–15.
- Nemes R, Fülesdi B, Pongrácz A, et al. Impact of reversal strategies on the incidence of postoperative residual paralysis after rocuronium relaxation without neuromuscular monitoring: a partially randomised placebo controlled trial. *Eur J Anaesthesiol*. 2017;34:609–616.
- Green LW, Ottoson JM, García C, Hiatt RA. Diffusion theory and knowledge dissemination, utilization, and integration in public health. Annu Rev Public Health. 2009;30:151–174.
- 25. Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. *J R Soc Med*. 2011;104:510–520.
- Rocuronium Package Insert. Available at: http://www.access-data.fda.gov/drugsatfda_docs/label/2008/078717s000lbl.pdf, Accessed May 11, 2016.

- Schultz P, Ibsen M, Østergaard D, Skovgaard LT. Onset and duration of action of rocuronium—from tracheal intubation, through intense block to complete recovery. *Acta Anaesthesiol Scand*. 2001;45:612–617.
- 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;98:1042–1048.
- 29. Baillard C, Clec'h C, Catineau J, et al. Postoperative residual neuromuscular block: a survey of management. *Br J Anaesth*. 2005;95:622–626.
- Todd MM, Hindman BJ. The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department: follow-up observations. *Anesth Analg*. 2015;121:836–838.
- 31. Della Rocca G, Iannuccelli F, Pompei L, Pietropaoli P, Reale C, Di Marco P. Neuromuscular block in Italy: a survey of current management. *Minerva Anestesiol*. 2012;78:767–773.
- 32. Brull ŠJ, Naguib M, Miller RD. Residual neuromuscular block: rediscovering the obvious. *Anesth Analg*. 2008;107:11–14.
- 33. Donati F. Neuromuscular monitoring: what evidence do we need to be convinced? *Anesth Analg*. 2010;111:6–8.
- 34. Kopman AF. Managing neuromuscular block: where are the guidelines? *Anesth Analg*. 2010;111:9–10.
- 35. Brull SJ, Naguib M. What we know: precise measurement leads to patient comfort and safety. *Anesthesiology*. 2011;115:918–920.
- 36. Hudson RJ. Neuromuscular monitoring should be required when neuromuscular blocking drugs are used: is it time to change the Canadian guidelines? Can J Anaesth. 2016;63:891.
- Lundstrøm LH, Duez CH, Nørskov AK, et al. Avoidance versus use of neuromuscular blocking agents for improving conditions during tracheal intubation or direct laryngoscopy in adults and adolescents. Cochrane Database Syst Rev. 2017;5:CD009237.
- Miskovic A, Lumb AB. Postoperative pulmonary complications. Br J Anaesth. 2017;118:317–334.
- Fleisher LA, Linde-Zwirble WT. Incidence, outcome, and attributable resource use associated with pulmonary and cardiac complications after major small and large bowel procedures. *Perioper Med (Lond)*. 2014;3:7.
- 40. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? *Anesth Analg*. 2015;120:51–58.
- Naguib M, Brull SJ, Johnson KB. Conceptual and technical insights into the basis of neuromuscular monitoring. *Anaesthesia*. 2017;72(suppl 1):16–37.
- 42. Ali HH, Utting JE, Gray C. Stimulus frequency in the detection of neuromuscular block in humans. *Br J Anaesth*. 1970;42:967–978.
- 43. Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block J. *Br J. Angesth*, 1971;43:473–477
- ual antidepolarizing block. I. *Br J Anaesth*. 1971;43:473–477. 44. Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block. II. *Br J Anaesth*. 1971;43:478–485.
- Viby-Mogensen J, Howardy-Hansen P, Chraemmer-Jørgensen B, Ording H, Engbaek J, Nielsen A. Posttetanic count (PTC): a new method of evaluating an intense nondepolarizing neuromuscular blockade. *Anesthesiology*. 1981;55:458–461.
- 46. Merton PA. Voluntary strength and fatigue. *J Physiol*. 1954;123:553–564.
- Stanec A, Heyduk J, Stanec G, Orkin LR. Tetanic fade and post-tetanic tension in the absence of neuromuscular blocking agents in anesthetized man. *Anesth Analg.* 1978;57:102–107.
- Kopman AF, Epstein RH, Flashburg MH. Use of 100-Hertz tetanus as an index of recovery from pancuronium-induced non-depolarizing neuromuscular blockade. *Anesth Analg*. 1982;61:439–441.
- Brull SJ, Silverman DG. Tetanus-induced changes in apparent recovery after bolus doses of atracurium or vecuronium. *Anesthesiology*. 1992;77:642–645.
- Dupuis JY, Martin R, Tessonnier JM, Tétrault JP. Clinical assessment of the muscular response to tetanic nerve stimulation. *Can J Anaesth*. 1990;37:397–400.
- 51. Werba A, Klezl M, Schramm W, et al. The level of neuromuscular block needed to suppress diaphragmatic movement during tracheal suction in patients with raised intracranial pressure: a study with vecuronium and atracurium. *Anaesthesia*. 1993;48:301–303.

- 52. Fernando PU, Viby-Mogensen J, Bonsu AK, Tamilarasan A, Muchhal KK, Lambourne A. Relationship between posttetanic count and response to carinal stimulation during vecuroniuminduced neuromuscular blockade. Acta Anaesthesiol Scand. 1987;31:593-596.
- 53. Brull SJ, Silverman DG. Pulse width, stimulus intensity, electrode placement, and polarity during assessment of neuromuscular block. Anesthesiology. 1995;83:702-709.
- 54. Rosenberg H, Greenhow DE. Peripheral nerve stimulator performance: the influence of output polarity and electrode placement. Can Anaesth Soc J. 1978;25:424-426.
- Caffrey RR, Warren ML, Becker KE Jr. Neuromuscular blockade monitoring comparing the orbicularis oculi and adductor pollicis muscles. Anesthesiology. 1986;65:95-97.
- 56. Donati F, Meistelman C, Plaud B. Vecuronium neuromuscular blockade at the diaphragm, the orbicularis oculi, and adductor pollicis muscles. Anesthesiology. 1990;73:870-875.
- 57. Thilen SR, Hansen BE, Ramaiah R, Kent CD, Treggiari MM, Bhananker SM. Intraoperative neuromuscular monitoring site and residual paralysis. Anesthesiology. 2012;117:964-972.
- 58. Donati F. Neuromuscular monitoring: more than meets the eye. Anesthesiology. 2012;117:934-936.
- 59. Ali HH, Savarese JJ, Lebowitz PW, Ramsey FM. Twitch, tetanus and train-of-four as indices of recovery from nondepolarizing neuromuscular blockade. Anesthesiology. 1981;54:294–297.
- Katz RL. Comparison of electrical and mechanical recording of spontaneous and evoked muscle activity. The clinical value of continuous recording as an aid to the rational use of muscle relaxants during anesthesia. Anesthesiology. 1965;26:204–211.
- 61. Engbaek J. Monitoring of neuromuscular transmission by electromyography during anaesthesia. A comparison with mechanomyography in cat and man. Dan Med Bull. 1996;43:301-316.
- Kopman AF. The dose-effect relationship of metocurine: the integrated electromyogram of the first dorsal interosseous muscle and the mechanomyogram of the adductor pollicis compared. Anesthesiology. 1988;68:604-607.
- 63. Engbaek J, Skovgaard LT, Friis B, Kann T, Viby-Mogensen J. Monitoring of the neuromuscular transmission by electromyography (I). Stability and temperature dependence of evoked EMG response compared to mechanical twitch recordings in the cat. Acta Anaesthesiol Scand. 1992;36:495-504
- 64. Kopman AF, Justo MD, Mallhi MU, Abara CE, Neuman GG. The influence of changes in hand temperature on the indirectly evoked electromyogram of the first dorsal interosseous muscle. Can J Anaesth. 1995;42:1090-1095.
- 65. Viby-Mogensen J, Jensen E, Werner M, Nielsen HK. Measurement of acceleration: a new method of monitoring neuromuscular function. Acta Anaesthesiol Scand. 1988;32:45-48.
- 66. Jensen E, Viby-Mogensen J, Bang U. The accelograph: a new neuromuscular transmission monitor. Acta Anaesthesiol Scand. 1988;32:49-52.
- 67. Suzuki T, Fukano N, Kitajima O, Saeki S, Ogawa S. Normalization of acceleromyographic train-of-four ratio by baseline value for detecting residual neuromuscular block. Br J Anaesth. 2006;96:44-47.
- 68. Kern SE, Johnson JO, Westenskow DR, Orr JA. An effectiveness study of a new piezoelectric sensor for train-of-four measurement. Anesth Analg. 1994;78:978-982.
- Motamed C, Kirov K, Combes X, Duvaldestin P. Comparison between the Datex-Ohmeda M-NMT module

- force-displacement transducer for monitoring neuromuscular blockade. Eur J Anaesthesiol. 2003;20:467-469.
- 70. Söderström CM, Eskildsen KZ, Gätke MR, Staehr-Rye AK. Objective neuromuscular monitoring of neuromuscular blockade in Denmark: an online-based survey of current practice. Acta Anaesthesiol Scand. 2017;61:619-626.
- 71. Indications of neuromuscular blockade in anaesthesia. Short
- text. *Ann Fr Anesth Reanim*. 2000;19(suppl 2):352s–355s.
 72. Checketts MR, Alladi R, Ferguson K, et al; Association of Anaesthetists of Great Britain and Ireland. Recommendations for standards of monitoring during anaesthesia and recovery 2015: Association of Anaesthetists of Great Britain and Ireland. Anaesthesia. 2016;71:85-93.
- 73. American Society of Anesthesiologists' Standards and Practice Parameters Committee. Standards for Anesthetic Monitoring. Available at: http://www.asahq.org/ search#q=STANDARDS%20FOR%20BASIC%20ANESTHETIC2 0MONITORING&sort=relevancy. Accessed November 21, 2017.
- 74. Engbaek J, Ostergaard D, Viby-Mogensen J. Double burst stimulation (DBS): a new pattern of nerve stimulation to identify residual neuromuscular block. Br J Anaesth. 1989;62:274-278.
- 75. Gupta DM, Boland RJ Jr, Aron DC. The physician's experience of changing clinical practice: a struggle to unlearn. Implement Sci. 2017;12:28.
- 76. Prasad V, Ioannidis JP. Evidence-based de-implementation for contradicted, unproven, and aspiring healthcare practices. Implement Sci. 2014;9:1.
- 77. McGill N, Yoon M. A quality improvement program involving protocolised reversal from neuromuscular block. Anaesthesia. 2017;72:1152–1153
- 78. Eichhorn JH, Cooper JB, Cullen DJ, Maier WR, Philip JH, Seeman RG. Standards for patient monitoring during anesthesia at Harvard Medical School. JAMA. 1986;256:1017-1020.
- 79. Butterly A, Bittner EA, George E, Sandberg WS, Eikermann M, Schmidt U. Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge. Br J Anaesth. 2010;105:304-309.
- 80. Berg H, Roed J, Viby-Mogensen J, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications. A prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. Acta Anaesthesiol Scand. 1997;41:1095-1103.
- 81. Grol R, Dalhuijsen J, Thomas S, Veld C, Rutten G, Mokkink H. Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. BMJ. 1998;317:858–861.
- 82. National Institute for Health Research. Getting evidence into practice. NIHR Centre for Reviews and Dissemination Effective Health Care Bulletin. 1999;5:1–16.
- 83. Chaillet N, Dubé E, Dugas M, et al. Evidence-based strategies for implementing guidelines in obstetrics: a systematic review. Obstet Gynecol. 2006;108:1234-1245.
- 84. Wyszewianski L, Green LA. Strategies for changing clinicians' practice patterns. A new perspective. J Fam Pract. 2000;49:461-464.
- 85. Gurses AP, Marsteller JA, Ozok AA, Xiao Y, Owens S, Pronovost PJ. Using an interdisciplinary approach to identify factors that affect clinicians' compliance with evidence-based guidelines. Crit Care Med. 2010;38:S282-S291.