Review Articles/Brief Reviews

Brief review: Neuromuscular monitoring: an update for the clinician

[Article de synthèse court : Monitorage neuromusculaire : une mise à jour pour le clinicien]

Thomas M. Hemmerling MD DEAA,*† Nhien Le*

Purpose: To review established techniques and to provide an update on new methods for clinical monitoring of neuromuscular function relevant to anesthesia.

Source: A PubMed search of relevant article for the period 1985–2005 was undertaken, and bibliographies were scanned for additional sources.

Principal findings: There is no substitute for objective neuromuscular monitoring; for research purposes, mechanomyography (MMG) is the gold standard; however, the most versatile method in the clinical setting is acceleromyography since it can be applied at various muscles and has a long track record of clinical utility. Kinemyography is valid to monitor recovery of neuromuscular transmission at the adductor pollicis muscle (AP), whereas phonomyography is easy to apply to various muscles and shows promising agreement with MMG. Monitoring of the corrugator supercilii muscle (CS) may be used to determine the earliest time for tracheal intubation as it reflects laryngeal relaxation better than monitoring at the AP. Recovery of neuromuscular transmission is best monitored at the AP, since it is the last muscle to recover from neuromuscular blockade (NMB). If train-of-four (TOF) stimulation is used, a TOF-ratio > 0.9 should be the target before awakening the patient. If surgery or the type of anesthesia necessitates NMB of a certain degree, e.g., TOF-ratio = 0.25, monitoring of muscles which best reflect the degree of NMB at the surgical site is preferable.

Conclusion: Objective methods should be used to monitor neuromuscular function in clinical anesthesia. Acceleromyography offers the best compromise with respect to ease of use, practicality, versatility, precision and applicability at various muscles. The CS is the optimal muscle to determine the earliest time for intubation, e.g., for rapid sequence induction.

CAN J ANESTH 2007 / 54: 1 / pp 58–72

***Objectif** : Faire le point sur les techniques établies et fournir une mise à jour sur les nouvelles méthodes de monitorage clinique de la fonction neuromusculaire pertinentes à l'anesthésie.*

***Source** : Une recherche PubMed d'articles pertinents de la période 1985-2005 a été effectuée, et des bibliographies ont été fouillées afin d'obtenir des sources supplémentaires.*

***Constatations principales** : Il n'existe pas de substitut pour le monitorage neuromusculaire objectif ; à des fins de recherche, la méchanomyographie (MMG) est l'étalon or (« gold standard ») ; l'accéléromyographie est la méthode la plus polyvalente dans un environnement clinique, étant donné qu'elle peut être appliquée à divers muscles et a depuis longtemps fait ses preuves d'utilité clinique. La kinémyographie est valable pour surveiller la récupération de la transmission neuromusculaire au niveau du muscle adducteur du pouce (AP), alors que la phonomyographie est facile à appliquer à divers muscles et démontre un accord prometteur avec la MMG. Le monitorage du muscle sourcilier (CS) peut être utilisé afin de déterminer le temps le plus court pour l'intubation trachéale, étant donné qu'il reflète la curarisation du larynx mieux que le monitorage de l'AP. La récupération de la transmission neuromusculaire est le mieux surveillée au niveau de l'AP, vu que ce muscle est le dernier à se rétablir d'un blocage neuromusculaire (BNM). Si une*

From the Neuromuscular Research Group (NRG), Department of Anesthesiology,* Montreal General Hospital, McGill University; and the Institut de Génie Biomédical,† Université de Montréal, Montreal, Quebec, Canada.

Address correspondence to: Dr. Thomas Hemmerling, Anaesthesia Department, McGill University Health Centre (MUHC), Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada. Phone: 514-934-1934, ext. 43795; Fax: 514-934-8249; E-mail: thomashemmerling@hotmail.com

Dr. Hemmerling is the recipient of the 2006 Bristol-Myers Squibb Canada/CAS Career Scientist Award in Anesthesia and Perioperative Medicine, which supports in part, his work in the field of neuromuscular research. Dr. Hemmerling has patents for phonomyography filed in Canada (Patent No. 2,415,173); and in the United States (Patent No. 10/730,811).

Accepted for publication May 18, 2005.

Revision accepted August 17, 2006.

Final revision accepted September 13, 2006.

stimulation en train-de-quatre (TOF) est utilisée, un ratio de TOF > 0,9 devrait être l'objectif avant de réveiller le patient. Si la chirurgie ou le type d'anesthésie nécessite un BNM d'un certain degré, par exemple, un ratio de TOF = 0,25, le monitorage des muscles qui reflète le mieux le degré de BNM au site chirurgical est préférable.

***Conclusion** : Des méthodes objectives devraient être utilisées pour le monitorage de la fonction neuromusculaire en anesthésie clinique. L'accéléromyographie offre le meilleur compromis si l'on considère la facilité d'utilisation, l'aspect pratique, la flexibilité, la précision ainsi que l'applicabilité à divers muscles. Le CS est le muscle optimal pour déterminer le temps le plus court pour l'intubation, par exemple lors d'une induction à séquence rapide.*

THE last 20 years have been exciting in neuromuscular research since new technologies for monitoring neuromuscular function have emerged. Several of the new technologies have direct clinical applications for routine perioperative management. Acceleromyography (AMG) and kinemyography (KMG) provide increasingly objective measures of neuromuscular function. More recently, phonomyography (PMG) was introduced, and this technique provides the clinician with the ability to discern the differential effects of neuromuscular blocking drugs on various muscle groups. A better understanding of how different muscles respond to muscle relaxants has also increased our knowledge of the pharmacodynamic profiles and potency of neuromuscular blockade drugs (NMBDs).

This review considers the benefits and limitations of currently available methods of monitoring neuromuscular function, and weighs the related technology and different stimulation possibilities. Finally, recommendations for monitoring neuromuscular function in routine daily practice are provided. Relevant articles were searched through PubMed for the period 1980–2005 using the following keywords and terms: "neuromuscular blockade"; "neuromuscular monitoring"; "mivacurium", "rocuronium", "cisatracurium", "succinylcholine", "vecuronium", "atracurium"; "neuromuscular blockade" + "larynx", "diaphragm", "adductor pollicis muscle", "corrugator supercilii muscle", "orbicularis oculi", "vastus medialis muscle", "flexor hallucis brevis muscle"; "mechanomyography", "acceleromyography", "electromyography", "kinemyography", "phonomyography", "acoustic myography"; "staircase effect". Screened articles which considered the pharmacodynamic variability of NMBDs and which recorded comparisons between the adductor pollicis muscle (AP) and the larynx, the corrugator supercilii muscle (CS), the orbicularis oculi muscle (OO) and/or the diaphragm were considered, and their bibliographies were scanned for additional sources.

Rationale for routine monitoring of neuromuscular function

There are several periods during the course of general anesthesia when the use of NMBDs is important and neuromuscular monitoring is necessary. Although clinical experience and some studies have shown that endotracheal intubation without the use of NMBDs is possible,[1–3] profound anesthesia is usually required and intubating conditions are less optimal as compared with complete neuromuscular blockade (NMB).[4] Mencke *et al.*[5] found in a double-blind controlled study that the use of atracurium during a propofol-fentanyl induction scheme improved the quality of intubating conditions and decreased postoperative hoarseness and vocal cord damage. The insertion of an endotracheal tube using NMBDs enhances its ease and safety, and reduces postoperative patient discomfort. Even laryngeal mask airway (LMA) insertion may be facilitated by using a submaximal dose of a NMBD.[6] Furthermore, intermittent positive pressure ventilation (IPPV) with an LMA and a sub-paralyzing dose of NMBD may facilitate mechanical ventilation and avoid air leakage with the danger of subsequent ventilation problems (decrease in tidal volumes, air obstruction due to vocal cord adduction).[7] However, one study has shown that when using the LMA with IPPV, NMB does not alter the incidence or severity of pharyngolaryngeal discomfort,[8] possibly because pharyngeal mucosal pressures are not influenced by NMB.[9]

Although clinical judgment of surgical conditions (e.g., adequate relaxation) can be subjective, recent studies have shown that NMBDs can improve surgical conditions, most specifically in abdominal surgery.[10,11] Neuromuscular blockade can be used to maintain a lighter plane of anesthesia; profound NMB can be useful for procedures such as intracranial surgery or complex eye surgery where even slight movement could result in critical events.

Probably, the most critical time to monitor neuromuscular function is at the end of surgery, prior to emergence from anesthesia. Use of a peripheral nerve stimulator is common in order to document the extent of recovery of neuromuscular function by either tactile or visual evaluation – however limited this method might be.[12,13] It has been shown that a train-of-four (TOF) ratio > 0.9 at the AP is necessary to achieve adequate airway protection in order to avoid postoperative atelectasis or pneumonia.[14,15] Eriksson *et al.*[14] found a significantly reduced upper

esophageal sphincter resting tone at TOF-ratios < 0.9, reduced muscle coordination and shortened bolus transit times at a TOF-ratio of 0.6 in 14 awake volunteers. Berg *et al.*[15] showed that TOF-ratios < 0.7 present a significant risk for the development of postoperative pulmonary complications following a variety of surgeries. To date, the absence of an ideal monitoring device has been one of the main reasons why many anesthesiologists do not routinely use an objective method to monitor neuromuscular function.

Techniques to monitor neuromuscular function

Clinical evaluation

Subjective evaluation consists of the clinical evaluation of the degree of relaxation based on the patient's ability to perform certain tasks or the tactile muscle response associated with evoked stimulation. Clinical evaluation is limited during general anesthesia, but can be used to determine the return of normal neuromuscular transmission following emergence from anesthesia. Although some tests such as sustained head-lift, leg-lift or hand-grip sustained for more than five seconds[16] can be quite reliable, they depend on the degree of consciousness and cooperation of the patient after general anesthesia. With optimal patient cooperation, failure to adequately perform these simple tests should lead the clinician to suspect residual NMB and initiate more objective testing.

Subjective monitoring of NMB is still the most widely used method of neuromuscular monitoring. Subjective monitoring is mostly used at the hand to evaluate the response of the AP, but also at the eyebrow to record the response of the CS or the OO. Although agreement between these subjective and objective methods depends on observer experience[17–19] (especially with AMG), at best, each method serves to count the number of TOF-responses. The ability to distinguish subjectively between TOF-ratios of 0.7, 0.8 or 0.9 using AMG, while important clinically, is limited. Although double-burst stimulation (DBS) (see below) might improve the clinical assessment, DBS cannot be a substitute for other objective methods, and does not facilitate precise titration of iterative doses of NMBDs to maintain a specified degree of paralysis during surgery.

Quantitative (objective) methods

MECHANOMYOGRAPHY (MMG)

If neuromuscular monitoring should reflect the degree of relaxation of a given muscle, then measuring the actual force is the best method to monitor NMB. Of all the monitoring methods, MMG requires the most stringent preparations and precautions: ideally, the muscle should be fixed in a specially moulded cast to prevent changes of position, and a constant pre-load should be applied according to the muscle site monitored and the size of the muscle (Figure 1). However, MMG is not free of limitations: drift can be a problem, the response does not return to the control amplitude; and even a slight detachment of the hand from the monitoring device can change the amplitude of the evoked signal. In general, MMG devices are awkward and bulky to prepare, require meticulous control of hand positioning, and can only be used to measure the response at the AP.

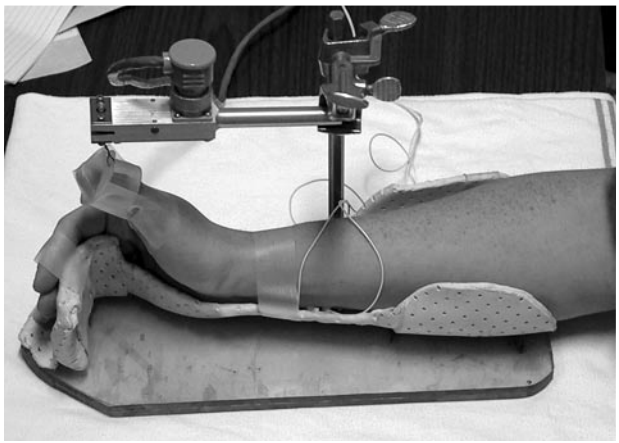

FIGURE 1 Setup for mechanomyographic monitoring. The arm should be placed in a pre-molded cast, the thumb attached to a force transducer with an adequate pre-load.

Other modalities exist which are MMG-alike, such as the balloon pressure method for monitoring either the larynx[20] or the CS.[21] These methods measure the actual force by indirect methods, such as the change of pressure exerted onto a balloon compressed by movement of the thumb or contraction of the CS. Again, these methods are not easy to apply in the clinical setting, and are reserved primarily for research purposes as a gold standard or reference against which other methods can be tested.

Electromyography (EMG)

Electromyography is the oldest method of neuromuscular monitoring[22] and is based on recording of the compound action potential after evoked stimulation of a motor nerve (Figure 2). Whether integrated or peak-to-peak amplitude is used to determine the power of the potential, the ability to use this method for routine monitoring is not influenced.[23] In general, EMG has been evaluated for most muscle sites of interest in

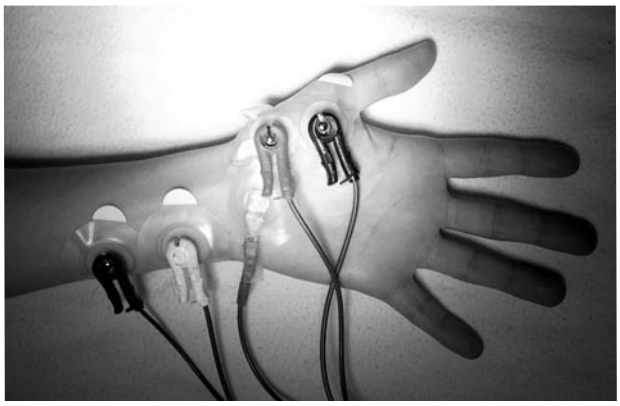

FIGURE 2 Stimulation of the ulnar nerve and electromyographic recording at the thenar area for detection of an evoked response of the adductor pollicis muscle. A neutral electrode needs to be placed in the middle of the hand. Recordings can be influenced by skin disease, such as found in Dupuytren's disease.

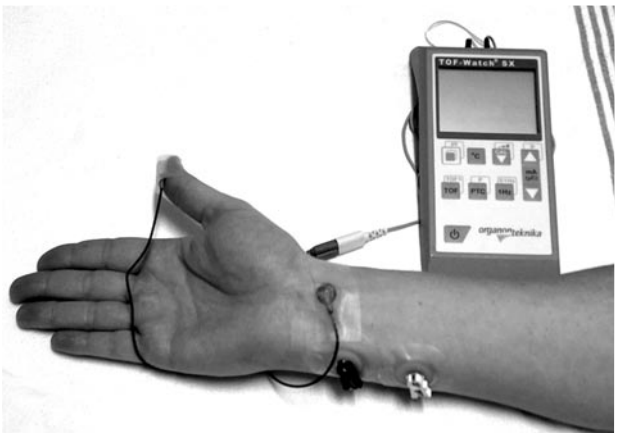

FIGURE 3 The piezoelectric probe of the acceleromyograph is attached to the tip of the thumb; stimulation of the ulnar nerve in standard fashion. For optimal results, the hand should be placed in a cast, as with mechanomyographic recordings.

research and clinical practice, such as the larynx,[24–26] the diaphragm,[27–29] the AP[30,31] and, with restrictions, the CS and the OO.[32] Electromyography of smaller muscles, however, is difficult because of the small action potentials created. Agreement with MMG can be a problem, and there are several studies which show that EMG and MMG cannot be used interchangeably.[33–37] Technical problems which arise with EMG include drift over time – the EMG potential does not return to control levels, failure to descend completely in fully relaxed muscles, and interference with other electronic devices. Despite these limitations, good correlation has been demonstrated in monitoring the effects of NMBDs at the diaphragm between manometrically measuring the pressure induced within the esophagus[38,39] (although cumbersome and invasive) and external EMG monitoring. Refinements of this monitoring technique have evolved with monitoring of the posterior diaphragm.[28]

Acceleromyography

Acceleromyography measures acceleration of a given end-organ, e.g., the thumb when moved by the AP. It is related to the actual force by the formula: force = mass × acceleration. Acceleromyography is easy to apply, can be used with data processing devices and is relatively inexpensive (Figure 3). Acceleromyography shows good agreement with MMG or EMG when the set-up has been carefully established.[40,41] However, its use at muscles other than the AP is limited: it cannot be used at the larynx or the the diaphragm, and only with difficulty at muscles which do not create a distinctive movement. Recently, it has been shown that use of AMG at the eye muscles, such as the CS, is limited, especially in detecting the maximum degree of NMB.[42] In general, the accuracy of AMG decreases when less movement, or acceleration, occurs at the end-organ, such as at the CS or the OO. Accuracy is dependent on the mass of the acceleromyographic probe. In a recent study, Kopman *et al.*[43] showed that the addition of an elastic preload to the thumb decreased the TOF variability without any effect on the relationship between twitch height and the TOF-ratio. At present, AMG is the most accurate and reliable monitoring method commercially available to measure NMB objectively in routine clinical settings.

Kinemyography

Recently, a neuromuscular monitoring device entered the market, integrated into the Datex Ohmeda Aestiva anesthetic machine (Datex Ohmeda Inc, Madison, WI, USA). The device uses KMG, and is based on measuring movement of the thumb (Figure 4). Kinemyography employs a piezo-electric transducer and consists of a moulded plastic device which mirrors the contour of the outstretched thumb and index finger. One study has shown that this device agrees reasonably with MMG for monitoring TOF-ratios, but other pharmacodynamic responses do not agree well with the MMG.[44] Although the Mechanosensor NMT device (Datex Ohmeda Inc, Madison, WI, USA) is practical in the clinical setting, its accuracy is not superior to that of AMG, and careful hand positioning is necessary to avoid artefacts. The response,

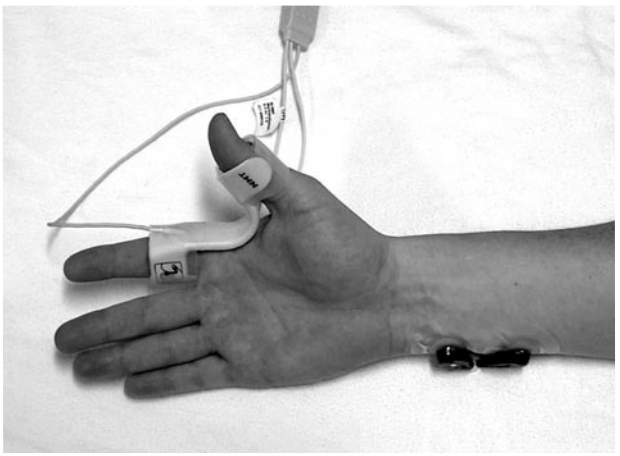

FIGURE 4 The NMT mechanosensor is a flexible plastic device, applied to the thumb to simulate a mechanomyography -like pre-load and needs to be attached with a regular gluing-tape. Monitoring is recorded in the form of columns and percentages of control amplitude.

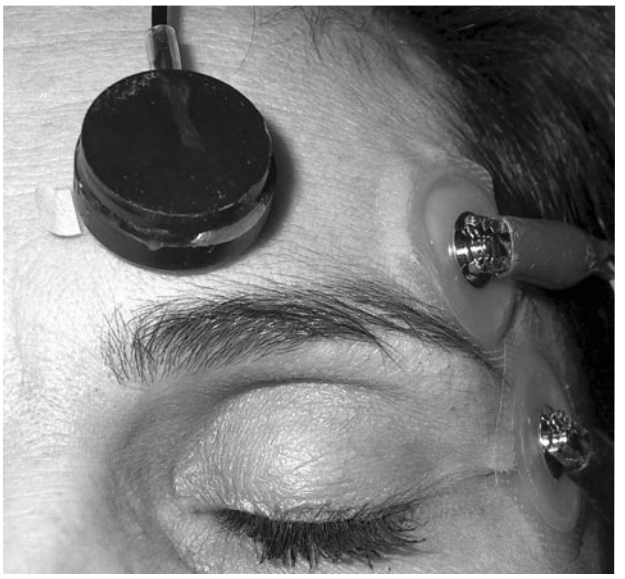

FIGURE 5 A small piezoelectric microphone is attached with self-adhesive tape onto the skin overlying the corrugator supercilii muscle for phonomyographic monitoring. Nerve stimulation of the facial nerve is performed in routine fashion using Ag AgCl-electrodes.

especially during recovery of neuromuscular function, can be misleading.[45]

Phonomyography

Phonomyography is based on the fact that contracting muscles evoke sounds of low frequencies which can be detected using special microphones. Muscle sounds were first described in 1665 by Grimaldi.[46] Recording muscle sounds involves specialized equipment. The most frequently used transducers are microphones (condenser or piezoelectric) or capacitance accelerometers.[47] The emission of sound waves is due to a spatial modification of the muscle during contraction. The signal can be recorded at the surface of the skin (Figure 5). It is important to have sufficient sensitivity to record very low frequencies; frequencies below 50 Hz represent approximately 90% of the signal power spectrum.[42] The signal is biphasic, and the peak-to-peak amplitude is the most useful measured parameter.

Initially, air-coupled, bulky microphones were used for PMG and one study showed very good agreement between PMG and MMG[48] whereas another study did not establish that agreement with MMG was sufficient for research purposes.[49] Limited ability of the air-coupled microphones to detect frequencies of 2–10 Hz might have been the reason for these contradictory results. It has been shown that the peak frequency of a typical signal is at 4–5 Hz and the maximum power occurs over a spectrum of frequencies up to 50 Hz.[42] Good to very good agreement with MMG or MMG-like methods has been shown for the adducting laryngeal muscles,[50] the CS,[21] and the AP.[51] In fact, at the CS, PMG was more sensitive in detecting the peak effect in comparison with AMG.[42] The advantage of PMG lies in the fact that it can be applied to every muscle site of interest and that it is an easy-to-apply, non-invasive method. A problem which needs resolution is the method of securing the microphone over the muscle of interest. When using tape, care needs to be taken to ensure that the microphone is not detached during the recording interval since change of contact surface or pressure between microphone and the skin or muscle changes the signal amplitude. This matter is of particular importance for single twitch stimulation. In a typical set-up, the hand is secured to an arm board and the microphone is taped to the thenar region for monitoring of the AP or first dorsal interosseus muscle. Phonomyography has been evaluated in several centres, but is not yet commercially available.

Stimulation patterns for monitoring neuromuscular function

All objective methods for assessment of neuromuscular function are based on the assessment of an evoked response to various patterns of stimulation of a motor nerve.

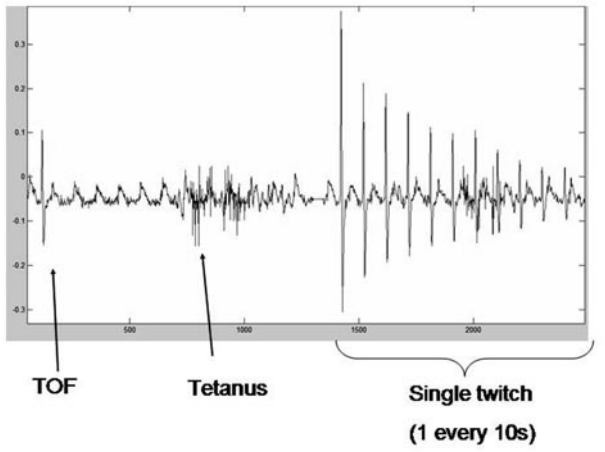

FIGURE 6 The most common stimulation patterns and the evoked responses of a partially relaxed muscle; only the first twitch response of train-of-four stimulation is visible; tetanus stimulation is performed, followed – three minutes later – by single-twitch stimulation to determine the post-tetanic count during profound relaxation.

The most important and widely used stimulation patterns are single-twitch stimulation, TOF-stimulation and post-tetanic facilitation (Figure 6).

Single-twitch stimulation

Single-twitch stimulation consists of a square wave stimulus lasting at least 0.2 msec. The amplitude of the stimulus can be varied using routine nerve stimulators; in general, the amplitude can be varied in increments up to 80 mA. Single-twitch stimulation can be accurately used in a research set-up so long as control amplitude returns to control values. However, since most clinicians still use tactile or visual evaluation of the degree of NMB, TOF-stimulation is the preferred pattern of stimulation.

Train-of-four stimulation

The delivery of square wave stimuli of 0.2 msec duration at 0.5 Hz has become the most commonly used stimulation mode. Typical fade of the TOF response defines competitive NMB by non-depolarizing NMBDs. Train-of-four monitoring is also very useful to evaluate the extent of intraoperative relaxation, with TOF-ratios between 0.15–0.25 usually indicating adequate surgical relaxation. A TOF-ratio > 0.9 has been shown to guarantee sufficient recovery of neuromuscular transmission for safe extubation of the trachea following surgery.[14]

Double-burst stimulation

Subjective evaluation of the TOF response at the AP has limited sensitivity to distinguish between a TOF-ratio of 0.7 or 0.9. To address this limitation, double-burst stimulation was introduced.[52,53] The preferred form of DBS (DBS 3, 3) consists of three stimuli of 0.2 msec duration at 50 Hz (20 msec intervals followed by three equal stimuli each lasting 750 msec). Although initially thought to improve the detection of fade, DBS might give the clinician a false sense of security in its ability to manually detect fade,[12] and DBS should not be considered a substitute for an objective quantitative method.

Tetanus and post-tetanic count

Before complete recovery of the TOF response, tetanic stimulation (stimulation at 50 Hz), followed more than three seconds later by single twitch stimulation at one second intervals, can be used to estimate the extent of deep NMB and time to recovery.[54] Several charts are available to correlate the numbers of single twitches to recovery from profound NMB.[55] Generally, a count > 10 is needed before recurrence of the first twitch of TOF stimulation can be assumed.

In general, objective monitoring methods use single twitch stimulation to determine onset of NMB; TOF stimulation every 12 sec is used to monitor the extent of NMB during surgery and recovery from general anesthesia.

Influence of monitoring site on the clinical response

Muscles differ in terms of onset, offset and peak effect of NMB. Several studies have investigated this phenomenon for various NMBDs. The Table groups several studies according to the pharmacodynamic variability of NMBDs. The following muscles are compared: AP *vs* larynx,[24,56–59] AP *vs* diaphragm,[38,60,61] AP *vs* OO,[62,63] AP *vs* larynx *vs* diaphragm,[27] AP *vs* CS *vs* larynx[64] and AP *vs* OO *vs* diaphragm[32] using the following NMBDs: atracurium,[38,59,62] rocuronium,[24,27,56,57,60,61,64] vecuronium,[32,62] succinylcholine,[27,38,56] mivacurium[62,63,65] and cisatracurium.[58,59] Monitoring solely muscles of the hand provides only a partial image of neuromuscular function of other major muscle groups. Therefore, it is important to establish which muscle to monitor for what purpose – monitoring NMB corresponding to a specific surgical site, monitoring NMB of the larynx, diaphragm or several peripheral muscles.

The staircase phenomenon and its importance for pharmacodynamic studies

The staircase phenomenon (or effect) describes the fact that repetitive stimulation of a motor nerve under anesthesia evokes muscle contractions of increasing amplitude of the corresponding muscle.[66,67] During repetitive stimulation, there is a significant increase in phosphorylation of the regulatory light chains of myosin which is proportional to the degree of the staircase phenomenon.[68,69] This increases calcium sensitivity and the force of the muscle contraction.[70] The staircase effect is an important issue for pharmacodynamic studies since it defines the duration of control stimulation before a stable response is established. Most human studies have investigated the staircase effect for hand muscles, especially the AP.[71–73] However, some animal studies have shown that the staircase effect is not uniform at all muscles. Van Lunteren and Vafaie[74] found that force potentiation in rats is more pronounced at the sternohyoid muscles than at the diaphragm. It is additionally known that the method of monitoring has an influence on the degree or duration of the staircase effect. Whereas the staircase phenomenon is positive for MMG[75] and AMG,[71] repetitive stimuli do not increase the size of the compound action potential and therefore do not change the signal height in EMG.[75] The staircase effect is equally found with one of the more novel methods, PMG.[76] However, Deschamps *et al.*[76] showed that the staircase effect is not uniform for all muscles: whereas hand muscles show the characteristic increase-plateau form of the staircase effect, this cannot be determined at the CS. The clinical impact of this finding is rather limited, but does stimulate discussion about the exact physiological basis of the staircase phenomenon.

Monitoring at sites other than the hand muscles

Several studies show that muscles around the eye, the CS and the OO, reflect accurately the response of laryngeal muscles or the diaphragm and recover faster from NMB than the AP.[77] Monitoring at the CS is especially helpful in types of surgery where relaxation of the diaphragm and more central muscles (e.g., abdominal muscles) are necessary. Nonetheless, more peripheral muscles (e.g., AP) need to be monitored in order to determine timely recovery of NMB. Alternatives to hand muscles include monitoring of the great toe or the vastus medialis muscle. However, there are limitations of these sites as described in the following sections.

Neuromuscular monitoring at the larynx

A monitoring method based on either MMG, EMG or PMG has been applied to the larynx. A mechanomyography-like method for the larynx consists of placing the cuff of the endotracheal tube between the vocal cords and measuring the force of the adducting laryngeal muscles via the degree of the pressure changes within the cuff.[20] A recent study has pointed out the importance of maintaining resting cuff pressure within the cuff in order to truly reflect the force of the adduction throughout NMB.[78] Electromyography of the larynx consists of using either a specialized endotracheal tube with incorporated wire electrodes [27] or a superficial electrode[26] attached circumferentially around the tube and placed between the vocal cords. Electromyography records the evoked compound action potential of several intrinsic laryngeal muscles, reflecting the neuromuscular action potential of adductors and the abductor of the larynx. A pharmacodynamic comparison of laryngeal EMG and the cuff pressure technique has not been done as yet.

Phonomyography shows good agreement with the standard cuff pressure method for monitoring NMB at the larynx.[50] By placing microphones on the laryngeal muscles, this technique is more convenient because of a more stable baseline, ease of signal analysis, absence of respiratory artefacts and little risk of accidental extubation or cuff displacement.

There are basically two sites for transcutaneous stimulation of the recurrent laryngeal nerve. The nerve can be stimulated either medially, between the jugular notch and the thyroid cartilage or, especially with use of a bipolar stimulation probe, just lateral to the sternocleidomastoid muscle in the tracheoesophageal groove.[61] In comparison to stimulation of the phrenic nerve, concomitant stimulation of the brachial plexus or the vagus nerve is rare.

In comparison to NMB at the AP, most studies confirm that onset and recovery of NMB at the larynx is faster. It seems that when sub-paralyzing doses of NMBDs are used, the peak effect at the larynx is less than at the AP. However, in doses which are generally used for endotracheal intubation ($> 2 \times ED_{95}$), there is no significant difference between the peak effects observed at the larynx and at the AP. Whereas faster onset of NMBDs at the larynx is most probably due to a more rapid "central" distribution of the drug, the reason for more rapid recovery is related primarily to morphological differences between the larynx and the AP (Table).

Neuromuscular monitoring of the diaphragm

Some studies have used EMG and MMG for monitoring the diaphragm. Electromyography using transcutaneous needles or superficial skin electrodes [27,29] has been applied to recording of NMB at the diaphragm

TABLE Pharmacodynamic variability of NMBDs according to monitoring site and method

Studies	*Method*	*NMBDs*	*Dosage* ($mg \cdot kg^{-1}$)	*Muscles*	*Onset and recovery parameters*				
					Onset (sec)	*T25% (min)*	*T75% (min)*	*T90% (min)*	*TOF 0.7 (min)*
Pansard *et al.*, 1987[38]	EMG	Atracurium	0.6	AP	181 ± 45	63 ± 13	78 ± 17		
				Diaphragm	137 ± 31	38 ± 7	49 ± 11		
								NA	NA
		Succinylcholine	0.8	AP	80 ± 24	7 ± 3	9 ± 4		
				Diaphragm	50 ± 11	5 ± 2	7 ± 3		
Donati *et al.*, 1990[32]	EMG	Vecuronium	0.04	AP	408 ± 30	NA	24.5 ± 5.0		
				Diaphragm	174 ± 36	NA	14.8 ± 3.0		
				OO	228 ± 36	NA	17.6 ± 8.0		
								NA	NA
			0.07	AP	378 ± 36	20.6 ± 2.6	35.0 ± 4.0		
				Diaphragm	132 ± 18	15.6 ± 2.5	26.0 ± 4.0		
				OO	204 ± 30	18.0 ± 2.7	28.7 ± 4.1		
Cantineau *et al.*, 1994[60]	EMG	Rocuronium	0.6	AP	80 ± 20	40 ± 13	56 ± 20	64 ± 21	
				Diaphragm	120 ± 62	23 ± 9	33 ± 13	35 ± 10	NA
Wright *et al.*, 1994[56]	EMG	Rocuronium	0.4	AP	155 ± 40	24 ± 7			
	`			Larynx	92 ± 29	NA			
			0.8	AP	74 ± 36	44 ± 10			
				Larynx	96 ± 45	25 ± 15	NA	NA	NA
			1.2	AP	65 ± 21	67 ± 25			
				Larynx	54 ± 30	43 ± 13			
		Succinylcholine	1.0	AP	56 ± 15	8 ± 2			
				Larynx	34 ± 12	4.3 ± 1.6			
Plaud *et al.*, 1996[65]	EMG	Mivacurium	0.07	AP	241 ± 79	13.2 ± 6.6	19.9 ± 6.8	23.3 ± 7.6	
				Larynx	151 ± 40	4.8 ± 1.7	8.7 ± 2.7	16.4 ± 4.9	
									NA
			0.14	AP	201 ± 59	16.2 ± 4.6	23.4 ± 6.2	27.4 ± 7.8	
				Larynx	137 ± 20	5.7 ± 2.1	12.8 ± 3.9	16.4 ± 4.9	
Rimaniol *et al.*, 1996[62]	AMG	Atracurium	0.3	AP	390 ± 150	32 ± 4	52 ± 13	60 ± 10	59 ± 13
				OO	385 ± 150	29 ± 11	44 ± 8	49 ± 10	43 ± 12
			0.5	AP	211 ± 270	53 ± 17	69 ± 22	77 ± 23	71 ± 17
				OO	170 ± 87	37 ± 18	58 ± 19	65 ± 21	56 ± 13
		Mivacurium	0.15	AP	232 ± 67	16 ± 6	27 ± 8	33 ± 9	28 ± 7
				OO	235 ±76	9 ± 5	17 ± 6	21 ± 4	15 ± 6
			0.25	AP	160 ± 30	22 ± 8	32 ± 10	37 ± 8	34 ± 9
				OO	90 ± 25	15 ± 7	25 ± 10	32 ± 8	19 ± 7
		Vecuronium	0.06	AP	269 ± 65	25 ± 6	41 ± 9	55 ± 10	52 ± 15
				OO	261 ± 88	20 ± 6	42 ± 15	49 ± 17	35 ± 8
			0.1	AP	174 ± 32	38 ± 7	67 ± 20	82 ± 23	78 ± 23
				OO	148 ± 38	43 ± 12	73 ± 22	82 ± 21	67 ± 18
Abdulatif *et al.*, 1997[63]	AMG	Mivacurium	0.2	AP	202.7 ± 37.2	12.9 ± 3.9	21.1± 5.1		
								NA	NA
				OO	130.4 ± 28.5	9.1 ± 3.2	16.2 ± 3.9		
Debaene *et al.*, 1997[57]	EMG	Rocuronium	0.75	AP	126 ± 33	5.6 ± 0.9	11.3 ± 1.8		17.9 ± 2.9
				Larynx	62 ± 16	2.4 ± 0.5	5.5 ± 2.0		NA
			1.5	AP	96 ± 20	10.2 ± 2.5	18.3 ± 5.2		30.4 ± 10.1
				Larynx	62 ± 13	3.7 ± 2.2	9.7 ± 3.7	NA	NA
			2.0	AP	82 ± 21	13.9 ± 2.6	25.0 ± 4.3		40.5 ± 5.1
				Larynx	52 ± 14	7.4 ± 3.6	16.7 ± 4.3		NA

TABLE *continued*

Studies	*Method*	*NMBDs*	*Dosage (mg·kg⁻¹)*	*Muscles*	*Onset and recovery parameters*				
					Onset (sec)	*T25% (min)*	*T75% (min)*	*T90% (min)*	*TOF 0.7 (min)*
Dhonneur *et al.*, 1999[27]	EMG	Rocuronium	0.6	AP	115 ± 21	29.5 ± 8.2	43.6 ± 9.4	49.1 ± 11.4	
				Larynx	124 ± 39	21.2 ± 5	31.0 ± 6.3	34.9 ± 7.6	
				Diaphragm	130 ± 44	17.9 ± 2.1	27.3 ± 3.8	30.4 ± 4.2	
									NA
		Succinylcholine	1.0	AP	54 ± 13	6.9 ± 2.6	8.3 ± 2.9	9.1 ± 3.0	
				Larynx	58 ± 10	4.3 ± 1.6	7.3 ± 3.1	8.3 ± 3.2	
				Diaphragm	57 ± 8	3.7 ± 1.5	6.2 ± 3.0	7.2 ± 3.5	
Kim *et al.*, 1999*[58]	EMG	Cisatracurium	0.1	AP	234 (180-288)	25.9 (19.8-32.1)	37.3 (32.1-42.5)	NA	NA
				Larynx	162 (132-192)	10.7 (7.6-13.8)	20.8 (15.6-26.1)		
Hemmerling *et al.*, 2000[24]	EMG	Rocuronium	0.6	AP	145 ± 48				
				Larynx	106 ± 38				
						NA	NA	NA	NA
			0.9	AP	99 ± 31				
				Larynx	64 ± 30				
Plaud *et al.*, 2001[64]	AMG	Rocuronium	0.6	AP	90 ± 35	33 ± 12		47 ± 15	
				CS	206 ± 72	17 ± 7	NA	34 ± 7	NA
				Larynx	181 ± 70	17 ± 10		33 ± 10	
Hemmerling *et al.*, 2002[61]	EMG	Rocuronium	0.6	AP	90 ± 17	25 ± 2			
				Diaphragm					
				Anterior	91 ± 15	14 ± 2	NA	NA	NA
				Posterior	93 ± 19	15 ± 3.5			
Kirov *et al.*, 2004[59]	EMG	Atracurium	0.5	AP	178 ± 47	45 ± 7	57 ± 6	61 ± 7	
				Larynx	140 ± 14	36 ± 7	46 ± 6	51 ± 4	
		Cisatracurium							NA
			0.1	AP	325 ± 88	38 ± 6	47 ± 5	53 ± 6	
				Larynx	196 ± 28	24 ± 6	38 ± 10	34 ± 9	

NMBDs = neuromuscular blockade drugs; NA = not available; AP = adductor pollicis muscle; CS = corrugator supercillii muscle; OO = orbicularis oculi muscle; AMG = acceleromyography; EMG = electromyography. All values are presented as mean ± SD. *For this article, values are presented as mean (95% confidence intervals).

after phrenic nerve stimulation.[61] The conventional site to record the electromyographic signals has been the seventh or eighth intercostal space, between the anterior axillary and the mid-clavicular line. A novel site at the patient's back has recently been used to monitor NMB [28,61] and has shown good agreement with *im* needle EMG of the diaphragm. Measurement of evoked transdiaphragmatic pressure as a form of indirect MMG of the diaphragm has also been used to evaluate NMB.[79] Two balloons are inserted into the esophagus to record pleural pressure and into the stomach to record intra-abdominal pressure. The balloons are connected with air-filled catheters to identical transducers. The transdiaphragmatic pressure (Pdi) is then obtained by electronic subtraction of gastric (alias intra-abdominal) and esophageal (alias pleural) pressure. This technique, however, is more invasive, more difficult to apply (it has to be recorded during resting end-expiration) and it requires bilateral phrenic nerve stimulation. Another disadvantage is that it cannot be used with an open abdominal cavity. Its advantage is the more MMG-alike approach, the transdiaphragmatic pressure being measured in the lower esophagus as a function of the force of diaphragmatic, yet non-isometric contraction. Two studies have shown good correlation between the transdiaphragmatic pressure method and EMG at the diaphragm.[80,81]

In general, most studies evaluating pharmacodynamic responses of NMBDs at the diaphragm have shown a similar time course and degree of NMB as responses at the larynx. The most difficult aspect of neuromuscular monitoring at the diaphragm is stimulation of the phrenic nerve. Stimulation must be done using either needles or a hand-held stimulator since the branches of the vagus nerve are deep; stabilization of the position of the stimulator is the main problem during continuous measurement evaluating onset or offset of NMB.

Neuromuscular monitoring of the CS

The CS is a small muscle around the eyebrow, responsible for vertical frowning. Recent studies have used AMG,[64,82] and PMG[21,42] to record the muscle response. Acceleromyography, although well established for the AP, might be problematic at this muscle because of the limited capability of the conventional acceleromyographic probe to detect acceleration created by this small muscle. The original acceleromyographic probe used with commercially available devices was originally designed for detecting acceleration created by the much larger AP. The TOF-watch SX (now distributed by Philips company, New York, NY, USA) has been designed with a different sensitivity set-up; the sensitivity can now be increased to 500 μC. A recent comparison of AMG and PMG to detect NMB at the CS has raised questions as to whether the TOF- watch SX is suitable to properly detect the neuromuscular response at this muscle.[42] Another recent study has tried to measure the actual force created by the CS using an air-filled balloon as a pressure transducer, and found good agreement between PMG and this MMG-like method.[21]

Monitoring NMB at the flexor hallucis brevis muscle (great toe)

Several studies have investigated the pharmacodynamic behaviour of the flexor hallucis brevis muscle.[83–87] with inconsistent results. The best agreement with the AP was observed in a study in infants[85] where there was no significant difference in onset time, peak effect or recovery from NMB of vecuronium 0.1 $mg \cdot kg^{-1}$ comparing the AP and the flexor hallucis brevis muscle. Both muscles were monitored using AMG. Most studies in adults have found similar peak effects but significantly longer onset times and shorter recovery of NMB at the great toe in comparison to the hand muscles.[83,84,86,87] Whereas higher blood flow to the hand[88] may possibly explain a faster onset at the hand muscles, morphological differences between the AP and the flexor hallucis brevis muscle might be responsible for the difference in recovery time. The AP consists of a higher content of type I (slow twitch) fibres than the flexor hallucis brevis muscle, which are known to be more sensitive to non-depolarizing NMBDs.[89] The pharmacodynamic differences between the great toe and the hand muscles limit the usefulness of the great toe as a replacement for monitoring NMB of the hand muscles in surgeries where access to the hand is impossible or movement of the hand is impaired.

The vastus medialis muscle

The vastus medialis muscle has been presented as an alternative monitoring site to the muscles of hand or foot. Saitoh *et al.*[90] showed that neuromuscular monitoring is possible at the vastus medialis muscle by stimulating the muscular branches of the femoral nerve, and quantifying the response of this muscle. In this study, the vastus medialis muscle, monitored by AMG, showed a faster onset of NMB than the AP. A possible explanation for these observations is a greater proportion of type II muscle fibres within the vastus medialis compared with the AP. A more recent study,[91] using PMG, confirmed the shorter onset time, a less pronounced maximum effect, and a more rapid recovery of NMB after mivacurium 0.2 $mg \cdot kg^{-1}$ at the vastus medialis muscle than at the AP. However, the vastus medialis muscle should be considered an alternative monitoring site for those surgeries where there is no access to hand or foot muscles, taking into account the considerable pharmacodynamic differences compared with the AP.

Recommendations for optimal monitoring of neuromuscular function

The concept of 'site-related' neuromuscular monitoring

The contribution of the anesthesiologist to achieve optimal surgical conditions is related to several factors, including sufficiently deep anesthesia, sufficient analgesia, as well as adequate NMB. "Adequate" NMB does not necessarily imply complete NMB, although successful outcomes of some surgeries may be related to profound NMB at the surgical site, e.g., retinal eye surgery, neurosurgery.

Since muscles react differently with respect to onset, recovery, and the degree of NMB, an important means of providing 'optimal' relaxation for the surgical site should consider monitoring muscles of the surgical site, or alternatively, muscles which adequately reflect NMB at the surgical site. There are few studies which have investigated this concept in practice. One might consider for example, monitoring the eye muscles of the opposite eye, or at least the facial muscle of

the contralateral site, to ensure profound NMB during retino-vitreal surgery. Monitoring of the AP does not reflect NMB at the eye muscles. Monitoring the AP as an indicator for relaxation of the thorax is also an inadequate. As described above, complete NMB at the AP does not necessarily mean complete NMB at the diaphragm. Monitoring NMB at the CS better reflects the degree of NMB at the surgical site during thoracic surgery.

The following concept is proposed: if surgery necessitates NMB of a certain degree, e.g., TOF 0.25, monitoring the muscle (or muscles) which best reflects the degree of NMB at the surgical site should be used. In general, for surgery of the upper or lower extremities, monitoring of the AP – or any other hand muscle - should be preferable. For surgery within the chest or abdomen where relaxation of the diaphragm is necessary, monitoring of the CS could be used.

Monitoring CS for intubation time

Current best evidence suggests that monitoring of the CS should be used to establish the earliest time for optimal conditions for tracheal intubation (e.g., for rapid sequence induction) as the CS reflects laryngeal relaxation better than monitoring of the AP.

Monitoring recovery from NMB

Recovery of neuromuscular transmission is best monitored at the AP since, in general, this is the last muscle group to recover from NMB. Train-of-four stimulation with a TOF-ratio > 0.9 indicates sufficient recovery of neuromuscular transmission for awakening the patient and ensuring safe tracheal extubation.

Subjective evaluation of NMB

Evaluation of clinical signs of recovered neuromuscular transmission after general anesthesia can be helpful, but requires that the patient is well awake, and should not replace objective neuromuscular monitoring.

Conclusion

There is no substitute for objective neuromuscular monitoring when muscle relaxants have been administered. At present, the most versatile technique to monitor neuromuscular function is AMG, since it can be applied at different muscles. Clinicians should be mindful of the pharmacodynamic studies which demonstrate the extent of inter-patient variability with respect to onset, peak effect and recovery from the effects of NMB. Because of this variability, and drug interactions, extensive clinical experience is not a substitute for objective assessment of NMB. The concept of "site-related" NMB may be useful to ensure more accurate monitoring of neuromuscular function, more accurate drug titration, and possibly, more optimal NMB at the surgical site.

References

1 *Erhan E, Ugur G, Gunusen I, Alper I, Ozyar B.* Propofol - not thiopental or etomidate - with remifentanil provides adequate intubating conditions in the absence of neuromuscular blockade. Can J Anesth 2003; 50: 108–15.

2 *Klemola UM, Mennander S, Saarnivaara L.* Tracheal intubation without the use of muscle relaxants: remifentanil or alfentanil in combination with propofol. Acta Anaesthesiol Scand 2000; 44: 465–9.

3 *Stevens JB, Wheatley L.* Tracheal intubation in ambulatory surgery patients: using remifentanil and propofol without muscle relaxants. Anesth Analg 1998; 86: 45–9.

4 *Lieutaud T, Billard V, Khalaf H, Debaene B.* Muscle relaxation and increasing doses of propofol improve intubating conditions. Can J Anesth 2003; 50: 121–6.

5 *Mencke T, Echternach M, Kleinschmidt S, et al.* Laryngeal morbidity and quality of tracheal intubation: a randomized controlled trial. Anesthesiology 2003; 98: 1049–56.

6 *Naguib M, Samarkandi AH.* The use of low-dose rocuronium to facilitate laryngeal mask airway insertion. Middle East J Anesthesiol 2001; 16: 41–54.

7 *Hemmerling TM, Michaud G, Deschamps S, Trager G.* 'Patients who sing need to be relaxed'--neuromuscular blockade as a solution for air-leaking during intermittent positive pressure ventilation using LMA. Can J Anesth 2005; 52: 549.

8 *Hemmerling TM, Beaulieu P, Jacobi KE, Babin D, Schmidt J.* Neuromuscular blockade does not change the incidence or severity of pharyngolaryngeal discomfort after LMA anesthesia. Can J Anesth 2004; 51: 728–32.

9 *Keller C, Brimacombe J.* Influence of neuromuscular block, mode of ventilation and respiratory cycle on pharyngeal mucosal pressures with the laryngeal mask airway. Br J Anaesth 1999; 83: 480–2.

10 *Williams MT, Rice I, Ewen SP, Elliott SM.* A comparison of the effect of two anaesthetic techniques on surgical conditions during gynaecological laparoscopy. Anaesthesia 2003; 58: 574–8.

11 *King M, Sujirattanawimol N, Danielson DR, Hall BA, Schroeder DR, Warner DO.* Requirements for muscle relaxants during radical retropubic prostatectomy. Anesthesiology 2000; 93: 1392–7.

12 *Fruergaard K, Viby-Mogensen J, Berg H, el-Mahdy AM.* Tactile evaluation of the response to double burst stimulation decreases, but does not eliminate, the problem

of postoperative residual paralysis. Acta Anaesthesiol Scand 1998; 42: 1168–74.

13 *Shorten GD, Merk H, Sieber T.* Perioperative train-of-four monitoring and residual curarization. Can J Anaesth 1995; 42: 711–5.

14 *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: 1035–43.

15 *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: 1095–103.

16 *Viby-Mogensen J.* Postoperative residual curarization and evidence-based anaesthesia. Br J Anaesth 2000; 84: 301–3.

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: 835–9.

18 *Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chraemmer-Jorgensen B.* Tactile and visual evaluation of the response to train-of-four nerve stimulation. Anesthesiology 1985; 63: 440–3.

19 *Saddler JM, Bevan JC, Donati F, Bevan DR, Pinto SR.* Comparison of double-burst and train-of-four stimulation to assess neuromuscular blockade in children. Anesthesiology 1990; 73: 401–3.

20 *Donati F, Plaud B, Meistelman C.* A method to measure elicited contraction of laryngeal adductor muscles during anesthesia. Anesthesiology 1991; 74: 827–32.

21 *Hemmerling TM, Michaud G, Babin D, Trager G, Donati F.* Comparison of phonomyography with balloon pressure mechanomyography to measure contractile force at the corrugator supercilii muscle. Can J Anesth 2004; 51: 116–21.

22 *Churchill-Davidson HC, Christie TH.* The diagnosis of neuromuscular block in man. Br J Anaesth 1959; 31: 290–301.

23 *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.

24 *Hemmerling TM, Schmidt J, Wolf T, Klein P, Jacobi K.* Comparison of succinylcholine with two doses of rocuronium using a new method of monitoring neuromuscular block at the laryngeal muscles by surface laryngeal electromyography. Br J Anaesth 2000; 85: 251–5.

25 *Hemmerling TM, Schmidt J, Wolf T, Wolf SR, Jacobi KE.* Surface vs intramuscular laryngeal electromyography. Can J Anesth 2000; 47: 860–5.

26 *Hemmerling TM, Schurr C, Walter S, Dern S, Schmidt J, Braun GG.* A new method of monitoring the effect of muscle relaxants on laryngeal muscles using surface laryngeal electromyography. Anesth Analg 2000; 90: 494–7.

27 *Dhonneur G, Kirov K, Slavov V, Duvaldestin P.* Effects of an intubating dose of succinylcholine and rocuronium on the larynx and diaphragm: an electromyographic study in humans. Anesthesiology 1999; 90: 951–5.

28 *Hemmerling TM, Schmidt J, Hanusa C, Wolf T, Jacobi KE.* The lumbar paravertebral region provides a novel site to assess neuromuscular block at the diaphragm. Can J Anesth 2001; 48: 356–60.

29 *Hemmerling TM, Schmidt J, Wolf T, Hanusa C, Siebzehnruebl E, Schmitt H.* Intramuscular versus surface electromyography of the diaphragm for determining neuromuscular blockade. Anesth Analg 2001; 92: 106–11.

30 *Harper NJ, Bradshaw EG, Healy TE.* Evoked electromyographic and mechanical responses of the adductor pollicis compared during the onset of neuromuscular blockade by atracurium or alcuronium, and during antagonism by neostigmine. Br J Anaesth 1986; 58: 1278–84.

31 *Pugh ND, Kay B, Healy TE.* Electromyography in anaesthesia. A comparison between two methods. Anaesthesia 1984; 39: 574–7.

32 *Donati F, Meistelman C, Plaud B.* Vecuronium neuromuscular blockade at the diaphragm, the orbicularis oculi, and adductor pollicis muscles. Anesthesiology 1990; 73: 870–5.

33 *Mellinghoff H, Diefenbach C, Arhelger S, Buzello W.* Mechanomyography and electromyography--2 competing methods of relaxometry using vecuronium (German). Anasth Intensivther Notfallmed 1989; 24: 57–9.

34 *Nakata Y, Goto T, Saito H, et al.* Comparison of acceleromyography and electromyography in vecuronium-induced neuromuscular blockade with xenon or sevoflurane anesthesia. J Clin Anesth 1998; 10: 200–3.

35 *Tammisto T, Wirtavuori K, Linko K.* Assessment of neuromuscular block: comparison of three clinical methods and evoked electromyography. Eur J Anaesthesiol 1988; 5: 1–8.

36 *Hofmockel VR, Benad G, Pohl B, Brahmstedt R.* Measuring muscle relaxation with mivacurium in comparison with mechano- and electromyography (German). Anaesthesiol Reanim 1998; 23: 72–80.

37 *Engbaek J, Roed J, Hangaard N, Viby-Mogensen J.* The agreement between adductor pollicis mechanomyogram and first dorsal interosseous electromyogram. A pharmacodynamic study of rocuronium and vecuronium. Acta Anaesthesiol Scand 1994; 38: 869–78.

38 *Pansard JL, Chauvin M, Lebrault C, Gauneau P, Duvaldestin P.* Effect of an intubating dose of succinylcholine and atracurium on the diaphragm and the adductor pollicis muscle in humans. Anesthesiology 1987; 67: 326–30.

39 *Chauvin M, Lebrault C, Duvaldestin P.* The neuromuscular blocking effect of vecuronium on the human diaphragm. Anesth Analg 1987; 66: 117–22.

40 *Kirkegaard-Nielsen H, Helbo-Hansen HS, Lindholm P, Pedersen HS, Severinsen IK, Schmidt MB.* New equipment for neuromuscular transmission monitoring: a comparison of the TOF-Guard with the Myograph 2000. J Clin Monit Comput 1998; 14: 19–27.

41 *Dahaba AA, Rehak PH, List WF.* Assessment of accelerography with the TOF-GUARD: a comparison with electromyography. Eur J Anaesthesiol 1997; 14: 623–9.

42 *Hemmerling TM, Donati F, Beaulieu P, Babin D.* Phonomyography of the corrugator supercilii muscle: signal characteristics, best recording site and comparison with acceleromyography. Br J Anaesth 2002; 88: 389–93.

43 *Kopman AF, Chin W, Cyriac J.* Acceleromyography vs. electromyography: an ipsilateral comparison of the indirectly evoked neuromuscular response to train-of-four stimulation. Acta Anaesthesiol Scand 2005; 49: 316–22.

44 *Motamed C, Kirov K, Combes X, Duvaldestin P.* Comparison between the Datex-Ohmeda M-NMT module and a force-displacement transducer for monitoring neuromuscular blockade. Eur J Anaesthesiol 2003; 20: 467–9.

45 *Hemmerling TM, Donati F.*The M-NMT mechanosensor cannot be considered as a reliable clinical neuromuscular monitor in daily anesthesia practice. Anesth Analg 2002; 95: 1826–7.

46 *Grimaldi FM.* Physicomathesis de Lumine. 1665.

47 *Frangioni JV, Kwan-Gett TS, Dobrunz LE, McMahon TA.* The mechanism of low-frequency sound production in muscle. Biophys J 1987; 51: 775–83.

48 *Dascalu A, Geller E, Moalem Y, Manoah M, Enav S, Rudick Z.* Acoustic monitoring of intraoperative neuromuscular block. Br J Anaesth 1999; 83: 405–9.

49 *Bellemare F, Couture J, Donati F, Plaud B.* Temporal relation between acoustic and force responses at the adductor pollicis during nondepolarizing neuromuscular block. Anesthesiology 2000; 93: 646–52.

50 *Hemmerling TM, Babin D, Donati F.* Phonomyography as a novel method to determine neuromuscular blockade at the laryngeal adductor muscles: comparison with the cuff pressure method. Anesthesiology 2003; 98: 359–63.

51 *Hemmerling TM, Michaud G, Trager G, Deschamps S, Babin D, Donati F.* Phonomyography and mechanomyography can be used interchangeably to measure neuromuscular block at the adductor pollicis muscle. Anesth Analg 2004; 98: 377–81.

52 *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: 274–8.

53 *Ueda N, Viby-Mogensen J, Engbaek J, et al.* New stimulation pattern for manual evaluation of neuromuscular transmission--double burst stimulation (DBS) (Japanese). Masui 1988; 37: 716–21.

54 *Viby-Mogensen J, Howardy-Hansen P, Chraemmer-Jorgensen B, Ording H, Engbaek J, Nielsen A.* Posttetanic count (PTC): a new method of evaluating an intense nondepolarizing neuromuscular blockade. Anesthesiology 1981; 55: 458–61.

55 *Muchhal KK, Viby-Mogensen J, Fernando PU, Tamilarasan A, Bonsu AK, Lambourne A.* Evaluation of intense neuromuscular blockade caused by vecuronium using posttetanic count (PTC). Anesthesiology 1987; 66: 846–9.

56 *Wright PM, Caldwell JE, Miller RD.* Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans. Anesthesiology 1994; 81: 1110–5.

57 *Debaene B, Lieutaud T, Billard V, Meistelman C.* ORG 9487 neuromuscular block at the adductor pollicis and the laryngeal adductor muscles in humans. Anesthesiology 1997; 86: 1300–5.

58 *Kim KS, Chung CW, Shin WJ.* Cisatracurium neuromuscular block at the adductor pollicis and the laryngeal adductor muscles in humans. Br J Anaesth 1999; 83: 483–4.

59 *Kirov K, Motamed C, Decailliot F, Behforouz N, Duvaldestin P.* Comparison of the neuromuscular blocking effect of cisatracurium and atracurium on the larynx and the adductor pollicis. Acta Anaesthesiol Scand 2004; 48: 577–81.

60 *Cantineau JP, Porte F, d'Honneur G, Duvaldestin P.* Neuromuscular effects of rocuronium on the diaphragm and adductor pollicis muscles in anesthetized patients. Anesthesiology 1994; 81: 585–90.

61 *Hemmerling TM, Schmidt J, Schurr C, Breuer G, Jacobi KE.* A comparison between anterior and posterior monitoring of neuromuscular blockade at the diaphragm: both sites can be used interchangeably. Anesth Analg 2002; 95: 940–3.

62 *Rimaniol JM, Dhonneur G, Sperry L, Duvaldestin P.* A comparison of the neuromuscular blocking effects of atracurium, mivacurium, and vecuronium on the adductor pollicis and the orbicularis oculi muscle in humans. Anesth Analg 1996; 83: 808–13.
63 *Abdulatif M, el-Sanabary M.* Blood flow and mivacurium-induced neuromuscular block at the orbicularis oculi and adductor pollicis muscles. Br J Anaesth 1997; 79: 24–8.
64 *Plaud B, Debaene B, Donati F.* The corrugator supercilii, not the orbicularis oculi, reflects rocuronium neuromuscular blockade at the laryngeal adductor muscles. Anesthesiology 2001; 95: 96–101.
65 *Plaud B, Debaene B, Lequeau F, Meistelman C, Donati F.* Mivacurium neuromuscular block at the adductor muscles of the larynx and adductor pollicis in humans. Anesthesiology 1996; 85: 77–81.
66 *Krarup C.* Enhancement and diminution of mechanical tension evoked by staircase and by tetanus in rat muscle. J Physiol 1981; 311: 355–72.
67 *Ritchie JM, Wilkie DR.* The effect of previous stimulation on the active state of muscle. J Physiol 1955; 130: 488–96.
68 *Moore RL, Houston ME, Iwamoto GA, Stull JT.* Phosphorylation of rabbit skeletal muscle myosin in situ. J Cell Physiol 1985; 125: 301–5.
69 *Manning DR, Stull JT.* Myosin light chain phosphorylation-dephosphorylation in mammalian skeletal muscle. Am J Physiol 1982; 242: C234–41.
70 *Persechini A, Stull JT, Cooke R.* The effect of myosin phosphorylation on the contractile properties of skinned rabbit skeletal muscle fibers. J Biol Chem 1985; 260: 7951–4.
71 *Kopman AF, Kumar S, Klewicka MM, Neuman GG.* The staircase phenomenon: implications for monitoring of neuromuscular transmission. Anesthesiology 2001; 95: 403–7.
72 *McCoy EP, Mirakhur RK, Connolly FM, Loan PB.* The influence of the duration of control stimulation on the onset and recovery of neuromuscular block. Anesth Analg 1995; 80: 364–7.
73 *Girling KJ, Mahajan RP.* The effect of stabilization on the onset of neuromuscular block when assessed using accelerometry. Anesth Analg 1996; 82: 1257–60.
74 *Van Lunteren E, Vafaie H.* Force potentiation in respiratory muscles: comparison of diaphragm and sternohyoid. Am J Physiol 1993; 264: R1095–1100.
75 *Krarup C.* Electrical and mechanical responses in the platysma and in the adductor pollicis muscle: in normal subjects. J Neurol Neurosurg Psychiatry 1977; 40: 234–40.
76 *Deschamps S, Trager G, Mathieu PA, Hemmerling TM.* The staircase phenomenon at the corrugator supercilii muscle in comparison with the hand muscles. Br J Anaesth 2005; 95: 372–6.
77 *Hemmerling TM, Donati F.* Neuromuscular blockade at the larynx, the diaphragm and the corrugator supercilii muscle: a review. Can J Anesth 2003; 50: 779–94.
78 *Girling KJ, Bedforth NM, Spendlove JL, Mahajan RP.* Assessing neuromuscular block at the larynx: the effect of change in resting cuff pressure and a comparison with video imaging in anesthetized humans. Anesth Analg 1999; 88: 426–31.
79 *Derrington MC, Hindocha N.* Measurement of evoked diaphragm twitch strength during anaesthesia. Adaptation and evaluation of an existing technique. Br J Anaesth 1988; 61: 270–8.
80 *McKenzie DK, Gandevia SC.* Phrenic nerve conduction times and twitch pressures of the human diaphragm. J Appl Physiol 1985; 58: 1496–504.
81 *Lebrault C, Chauvin M, Guirimand F, Duvaldestin P.* Relative potency of vecuronium on the diaphragm and the adductor pollicis. Br J Anaesth 1989; 63: 389–92.
82 *Hemmerling TM, Schmidt J, Hanusa C, Wolf T, Schmitt H.* Simultaneous determination of neuromuscular block at the larynx, diaphragm, adductor pollicis, orbicularis oculi and corrugator supercilii muscles. Br J Anaesth 2000; 85: 856–60.
83 *Saitoh Y, Fujii Y, Takahashi K, Makita K, Tanaka H, Amaha K.* Recovery of post-tetanic count and train-of-four responses at the great toe and thumb. Anaesthesia 1998; 53: 244–8.
84 *Kitajima T, Ishii K, Kobayashi T, Ogata H.* Differential effects of vecuronium on the thumb and great toe as measured by accelography and electromyography. Anaesthesia 1995; 50: 76–8.
85 *Kitajima T, Ishii K, Ogata H.* Assessment of neuromuscular block at the thumb and great toe using accelography in infants. Anaesthesia 1996; 51: 341–3.
86 *Heier T, Hetland S.* A comparison of train-of-four monitoring: mechanomyography at the thumb vs acceleromyography at the big toe. Acta Anaesthesiol Scand 1999; 43: 550–5.
87 *Kern SE, Johnson JO, Orr JA, Westenskow DR.* Clinical analysis of the flexor hallucis brevis as an alternative site for monitoring neuromuscular block from mivacurium. J Clin Anesth 1997; 9: 383–7.
88 *Goat VA, Yeung ML, Blakeney C, Feldman SA.* The effect of blood flow upon the activity of gallamine triethiodide. Br J Anaesth 1976; 48: 69–73.
89 *Johnson MA, Polgar J, Weightman D, Appleton D.* Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. J Neurol Sci 1973; 18: 111–29.
90 *Saitoh Y, Nakajima H, Hattori H, Aoki K, Katayama T, Murakawa M.* Neuromuscular blockade can be

assessed accelerographically over the vastus medialis muscle in patients positioned prone. Can J Anesth 2003; 50: 342–7.

91 *Michaud G, Trager G, Deschamps S, Hemmerling TM.* Monitoring neuromuscular blockade at the vastus medialis muscle using phonomyography. Can J Anesth 2005; 52: 795–800.

APPENDIX – List of definitions:

1. *Neuromuscular blockade:* Neuromuscular blockade is one of the three essential parts of general anesthesia. Monitoring of neuromuscular blockade consists either in having the patient perform contractions of certain muscles or muscle groups, such as hand squeezing or head lifting, or stimulation of a motor nerve and determining the evoked muscle response.
2. *Mechanomyography:* A quantitative method of assessing neuromuscular function which measures the force of a specific muscle using a force transducer.
3. *Electromyography:* A quantitative method of assessing neuromuscular function which records the compound action potential of a given muscle after evoked stimulation of a motor nerve.
4. *Acceleromyography (also known as accelerometry):* A quantitative method of assessing neuromuscular function which measures the acceleration of a given end-organ after contraction of the equivalent muscle, e.g., thumb after contraction of the adductor pollicis muscle. It is related to the actual force by the formula: force = mass × acceleration.
5. *Kinemyography:* A quantitative non-invasive method of assessing neuromuscular function using a piezoelectric transducer. A moulded plastic device fits between the thumb and index finger and measures deflection of the transducer in response to end-organ muscle contraction.
6. *Phonomyography:* A quantitative method of assessing neuromuscular function which measures low frequency acoustic waves created by muscle contraction. The acoustic amplitude is proportional to the amplitude of the contraction force (not yet commercially available).
7. *Single twitch stimulation:* A single, 0.2 msec square wave stimulus applied to a motor nerve.
8. *Train-of-four stimulation:* Stimulation consisting of 4 square wave stimuli of 0.2 msec duration at 0.5 Hz, applied to a motor nerve on an iterative basis or at regular intervals of 12 sec.
9. *Train-of-four ratio:* The ratio of the peak-to-peak amplitude of the fourth twitch in comparison to the first twitch response. This ratio permits calculation of the duration of action or the recovery from non-depolarizing blocking drugs
10. *Double-burst stimulation:* A method to evaluate recovery from the effects of neuromuscular blockade drugs consisting of three stimuli of 0.2 msec duration at 50 Hz, with an interval of 20 msec, followed by three equal stimuli of 750 msec.
11. *Tetanus and post-tetanic count:* Tetanic stimulation is stimulation of a peripheral motor nerve at high frequencies, most commonly at 50 Hz. Tetanic stimulation for five seconds, followed (3–5 sec later) by single-twitch stimulation at 1 Hz is used to determine recovery of neuromuscular transmission after profound non-depolarizing neuromuscular block (an absent response to train-of-four stimulation).
12. *Staircase phenomenon:* A phenomenon which describes the fact that repetitive stimulation of a motor nerve evokes muscle contractions of increasing amplitude in the corresponding muscle.