Anaesth Intensive Care 2002; **30:** 123-133

Reviews

Monitoring Neuromuscular Transmission

T. A. TORDA*

The Discipline of Anaesthesia, Intensive Care and Emergency Medicine, Clinical School of Medicine, Prince of Wales Hospital, University of New South Wales

SUMMARY

Persistent neuromuscular blockade is not uncommon in the recovery room and contributes to postoperative morbidity and possibly mortality. The use of neuromuscular monitoring and intermediate rather than long-acting neuromuscular blocking drugs have been shown to reduce its incidence. Clinically available methods of detecting and quantitating neuromuscular blockade are reviewed. The writer concludes that such monitoring should be routine when neuromuscular blocking drugs are used.

Key Words: MONITORING: neuromuscular transmission, blockade. NEUROMUSCULAR BLOCKADE: monitoring

Why monitor neuromuscular transmission or neuromuscular blockade (NMB)? To answer this, we should ask another question: Why do we use neuromuscular blocking drugs (NMBD) and what, precisely, do we want to achieve by their use?

1. To obtain good intubating conditions, rapidly and without unduly deep anaesthesia.
2. To provide good operating conditions with easy surgical access to body cavities and easy manipulation of the periphery when required.
3. Occasionally, when even slight movement may put the patient or the operative result at risk, profound paralysis offers a second "line of defence" to the provision of adequate anaesthetic depth.

There is a price to achieving these objectives. The use of NMBD may increase the liability to adverse outcomes[1-4]. Monitoring, therefore, must assist in enhancing safety in the following ways:

1. Monitoring can be helpful to show that the laryngeal adductors are ready for intubation after the initial dose of NMBD. This may reduce intubation trauma (T. Mencke et al, Intubation associated vocal cord dysfunction—a randomised placebo controlled trial. 7th International Neuromuscular Meeting, Belfast, June, 2001).
2. It is necessary in order to ensure that neuromuscular blockade (NMB) is rapidly and reliably reversible at the end of the operation.
3. It is also needed to ensure that the patient has normal function of all muscles, when delivered to the recovery room.

For economic reasons, as well as to ensure ready reversibility, it is desirable to achieve the goals of NMB using a minimum quantity of drug. Monitoring also assists this objective.

To reliably achieve these aims, monitoring the effect of the neuromuscular blocking drugs is essential. We know that "clinical impression" or "feel of the breathing bag" does not prevent residual neuromuscular blockade in the recovery room[5-7]. The variability of the response to NMBD is such that average times of recovery are poor guides to their dosage. For example, 0.1 $mg.kg^{-1}$ of d-tubocurarine caused no detectable effect in 6% and complete NMB in 7% of subjects receiving the dose, with effect between the two extremes in the remainder[8].

The role of NMBD in providing good intubating conditions is not as well investigated as it could be. It can be argued that anaesthesia sufficiently deep to prevent marked autonomic response to intubation will already provide adequate intubating conditions and many studies, especially of NMBDs, are performed with tracheal intubation preceding the administration of NMBD. It has also been shown that waiting three minutes after the NMBD

*M.D., B.S., F.A.N.Z.C.A., F.F.I.C.A.N.Z.C.A., F.F.A.R.C.S., Dip.Amer.Bd. Anaesthesiology, D.A.(Eng), Academic Head, Clinical Program in Anaesthesia and Intensive Care, Prince of Wales Hospital, Sydney. Professor of Anaesthesia and Intensive Care, University of New South Wales.

Address for reprints: Dr T. A. Torda, 38 Epping Road, Double Bay, N.S.W. 2028.

Accepted for publication on December 5, 2001.

administration will ensure near optimal paralysis of the laryngeal adductors without use of a monitor[9]. On the other hand, not many anaesthetists are willing to wait three minutes after induction, before introducing the tracheal tube.

It is usually agreed that 80-95% NMB, measured at the adductor pollicis (AP), is compatible with good operating conditions[10]. Therefore, even if total paralysis of the laryngeal adductors is required for easy intubation, maintenance of good operating conditions only requires about 90% blockade. To ensure ready reversibility of the NMB and the use of minimal quantities of NMBD, it seems logical not to use drug doses that induce deeper paralysis. This is facilitated by continuous monitoring and the use of small bolus doses or continuous infusions and makes measurement rather than tactile or visual evaluation of NMB desirable even though the appearance of the second response to train-of-four (TOF) stimulation coincides with about 20% NMB[11] and can serve as the indication for the next dose of NMBD.

Reversibility of non-depolarizing or competitive NMB depends on the concentration of NMBD at the effect site. When the concentration is such that there is about 20% twitch response or there are two responses present to each TOF train, blockade is usually rapidly antagonized by moderate doses of anticholinesterases[12]. Blockade deeper than this can lead to slow reversal or even the inability to reverse. There may also be a possible risk of re-curarization, especially if edrophonium is used for reversal. Monitoring should ensure that when the time for termination of NMB comes at the end of a case, reversal is prompt and effective.

Finally, the important question of persistent NMB needs be addressed. That is the problem of patients in the recovery room, with significant impairment of muscle power. Even with tactile or visual monitoring of evoked contractions, this may be a frequent event, which can be linked with increase in postoperative respiratory complications. With the anaesthetist's decision concerning adequate reversal based on "clinical impression", when no neuromuscular monitoring was used, of 72 patients, 68 were sufficiently recovered from anaesthesia to have their ability to perform a five-second head-lift test. Sixteen (24%) were unable to do this. Of the 72 patients 30 (42%) had TOF ratios <0.7, and 16 (22%), less than 0.6[5]. Other studies have shown similar results[13,14]. Replacement of long-acting NMBD by intermediate-acting drugs has not eliminated the problem[6,14] and it has been repeatedly shown that tactile or visual monitoring of the evoked response may reduce the incidence but also fails to eliminate the problem of partially paralysed patients in the recovery room[15,16].

In fact, what constitutes adequate recovery is in some dispute. The commonly accepted figure of 0.7 for the TOF ratio of the AP as "adequate reversal" appears to have been introduced about 25 years ago[17,18.] More recent work has called this "standard" into serious doubt. The criteria for choosing 0.7 as the critical ratio were that patients were able to produce peak inspiratory pressure of –25 cm H_2O and that their ventilation was normal. Swallowing and coughing, however, requires better neuromuscular recovery, equivalent to an inspiratory pressure of –45 cm H_2O[19]. The group from the University of Copenhagen, which is often quoted in this review, suggested 0.8 as the minimum adequate level of recovery[20]. Bevan has suggested that upper airway obstruction was possible following small doses of NMBD and may cause morbidity[21]. Ericsson et al[22] have shown that at TOF ratio of the AP of 0.7 there is significant weakness of the muscles of swallowing and contrast media entered the laryngeal vestibule in 25% of subjects under the study conditions. They concluded that patients with TOF ratio <0.9 are at increased risk of pulmonary aspiration. Another possible source of adverse effects is the demonstrated 25% reduction in hypoxic respiratory response following partial NMB[23] with the TOF ratio at 0.7. The significance of partial paralysis as a risk factor in postoperative pulmonary complications has been prospectively documented[24].

EVALUATION OF NEUROMUSCULAR TRANSMISSION AND BLOCKADE

Neuromuscular blockade can be measured in a number of ways. The simplest methods depend on recording voluntary muscle power such as handgrip or vital capacity, but these tests cannot be applied to anaesthetized patients. Assessment of NMB in anaesthetized subjects is therefore based on responses evoked by nerve stimulation. These responses can be estimated clinically by observation or feel but are much more accurately evaluated by measurement.

Clinical evaluation

When the patient is able to co-operate, a number of traditional clinical tests, some not requiring any special equipment can be performed to determine whether there is significant residual curarization. According to Viby-Mogensen, some of these commonly used tests are not reliable[25].

In an important study, however, Kopman et al[26] showed that when the TOF ratio was <0.7, five-

TABLE 1

Reliability of clinical signs to demonstrate reversal of neuromuscular blockade. (After J. Viby-Mogensen et al[22])

Reliable	Unreliable
Sustained head-lift 5 s	Sustained eye-opening
Sustained leg-lift 5 s	Protrusion of the tongue
Sustained hand-grip 5 s	Arm lift to opposite shoulder
Tongue depressor test[23]	Normal vital capacity
Maximum insp. pres. = <-50 cm H_2O	Maximum insp. pres. = <-25 cm H_2O

second head-lift was accomplished by 9 of 10 subjects and five-second leg-lift by 10 of 10. This suggests that either the standard of TOF ratio of 0.7 corresponding to adequate recovery, or these tests were inadequate. The tongue depressor test suggested in that paper simply required the subject to grip a wooden tongue depressor with their incisor teeth and not allow the investigator to pull it clear. This was generally accomplished at TOF ratio >0.85. In general, this paper also calls into doubt the accepted figure of 0.7 TOF ratio, for adequate reversal.

Tactile or visual evaluation of the evoked response

Tactile or visual assessment of evoked responses, either of the AP, the orbicularis oculi or elsewhere, are commonly used to evaluate neuromuscular response even though their reliability is not great[20]. Tactile assessment of the TOF in inexperienced hands may fail to detect fade when the TOF ratio is as low as 0.1-0.2 and in experienced hands, 0.4[27-29]. Responses of the orbicularis oculi are usually evaluated visually, although accelerometry is possible, at least in some patients. Such evaluation probably should be interpreted in terms of TOF count rather than attempting to assess fade. The TOF count can be used to time intubation, predict the need for repeat doses or to predict reversibility of the block. It is, however, not a measure of adequate reversal.

Double-burst stimulation was designed to enhance tactile assessment of NMB[30]. It appears to be superior to the TOF pattern for this purpose but still fails to eliminate the problem of postoperative residual NMB[14].

Electromyography

The first method of recording and measuring of NMB for clinical use in anaesthesia was electromyography (EMG). It was introduced by Churchill-Davidson and Christie[31] in 1959, who published recordings of the compound action potential of the AP and changes induced by NMBD. In this context, EMG records the compound action potential of the selected muscle, in response to supramaximal stimulation of the nerve supply. The recording can be the peak-to-peak amplitude, or the rectified area of the response curve (the integrated EMG). Although on theoretical grounds integrated EMG appears preferable, in practice the two appear to be equally good for monitoring of NMB[32]. The biggest practical problem with electromyography (EMG) is electromagnetic interference, but by sophisticated gating and filtering techniques, clinically useful monitoring devices such as the Relaxograph® (Datex) have been developed commercially. Electromyography is especially useful for research situations where the investigated muscle such as the adductors of the larynx, the facial muscles or the diaphragm cannot readily be connected to force, acceleration or piezoelectric transducers. Another advantage is that fixation of the monitored muscle is not as critical as for measurement of force. Electromyography can also be used to investigate spontaneous muscle activity such as breathing.

Comparison with mechanomyography (MMG) has shown that agreement between the two methods is generally good, but the two cannot be used interchangeably[17,33-35]. In recordings of unprocessed EMG, usually the amplitude failed to reach 0 even when no mechanical response was detectable. This may have been due to electronic noise, the nerve action potential or both. There may also be problems with drift over time in the EMG and failure to return to control amplitude[36].

Force of contraction

The gold standard of measurement of neuromuscular response is recording of the force of contraction evoked by supramaximal peripheral nerve stimulation in a selected muscle (mechanomyography, MMG), despite the fact that theoretically, at least, changes in muscle contractility as well as NMB could affect the response. The method requires rigid fixation of the monitored muscle, with constant resting fibre length (pre-load) and maintenance of muscle temperature within limits for accurate results[37,38]. Commercial force-displacement transducers were initially used, in conjunction with rigid arm-boards to fix the position of the arm and hand to assure the constant pre-load necessary for consistent response. The Myograph 2000® (Biometer) is probably the best known of such dedicated systems and was designed to measure the isometric response of the AP in response to stimulation of the ulnar nerve.

In fact, it is quite easy to put together inexpensive systems to monitor MMG with reasonable accuracy.

Probably the simplest is the use of a syringe, taped into the hand of the patient and connected to a manometer[39]. A somewhat more sophisticated version of the device uses a pressure transducer connected to any invasive blood pressure monitor instead of a manometer to record response[40,41]. Another ingenious system is devised from a drip set wrapped around the subject's hand, connected to a pressure transducer[42].

One step more complex, but still quite inexpensive, is to build a force-displacement transducer[43]. If the impedance of the elements is appropriately chosen to roughly match a blood pressure transducer (200-300), this also can be plugged into a blood pressure monitor.

Accelerometry

Basic physics tell us that

Force = Mass x Acceleration

The mass moved by the monitored muscle will not change appreciably during monitoring. Acceleration, therefore, must be proportional to force. These devices, such as the TOF-Guard® (Biometer), TOF-Watch® and TOF-Watch SX® (Organon) are easy and convenient to use, less expensive than dedicated force-displacement systems and the "SX" interfaces readily with personal computers for data storage and processing. Their agreement with other methods has been well tested[44,45]. It is claimed that their use can eliminate the risk of postoperative residual curarization[46].

Piezoelectric movement detector

Datex markets a monitor, which fits as a module into their AS/3 and S5 monitoring systems (the NMT module), which measures isotonic response of the thumb to stimulation. It uses a piezoelectric transducer like another commercially available system, the ParaGraph®[47,48]. The agreement between piezoelectric systems and MMG, however, was quite poor. The writer has extensive experience with the Datex NMT® and found it excellent for clinical monitoring, but for use in research it requires validation. The NMT module offers the user the choice of TOF, double-burst stimulation or post-tetanic count as stimulation modes and also offers EMG as an alternative recording system.

Acoustic Monitoring

When muscle contracts, low frequency "sound" is emitted. The original paper placed this in the 60-100 Hz band, which could be recorded by an air-coupled microphone applied to the thenar eminence. The root mean square of the signal amplitude was compared to the EMG, MMG and the accelerogram. The limits of agreement were about 40%[49]. A more recent study suggested that peak power of the signal was at lower frequency, <20 Hz, and that the method was suitable for monitoring the corrugator supercilii (T. H. Hemmerling et al., Phonomyography of the corrugator supercilii muscle: Signal characteristics and best monitoring site. 7th International Neuromuscular Meeting, Belfast, June 2001). The usefulness of this method for clinical monitoring or research remains to be determined.

Patterns of stimulation

Twitch stimulation

Single stimuli at various time intervals were first used for evaluating neuromuscular transmission. The first nerve stimulator, designed for clinical monitoring of NMB was the Block-Aid® (Burroughs-Wellcome)[50], which was an extremely useful and inexpensive device for tactile or visual evaluation of the twitch and tetanic responses and post-tetanic facilitation. Although designed to output a 0.2 ms stimulus, in fact this was followed by a lower voltage but prolonged 5 ms inverted output, due to the use of a transformer in the output circuit. This had the effect of a short tetanus and appeared to be chiefly responsible for the evoked muscle contraction[51]. The preferred stimulator output for single twitch recording is square wave, 0.2 ms impulses[34]. Above 0.3 ms impulse duration, repetitive firing of some of the muscle fibres may occur and this would introduce the refractory period of the system as a possible variable affecting the response amplitude. Magnetic induction has also been used for peripheral nerve stimulation[52]. Amplitude of the twitch response is maximal at stimulation rate of 0.1 Hz or less and is reduced in the presence of competitive NMB as the stimulation rate increases[53] (Figure 1). Single twitch stimulation does not sufficiently stress neuromuscular transmission to be useful as a clinical test for reversal of paralysis as even 100% recovery does not assure normal muscle function[54].

Tetanic stimulation and post-tetanic facilitation

Tetanic stimulation is painful and therefore it is not useful in testing neuromuscular transmission in conscious subjects. With unblocked neuromuscular transmission, tetanus at 50 Hz is well maintained but in the presence of non-depolarizing NMB, it fades

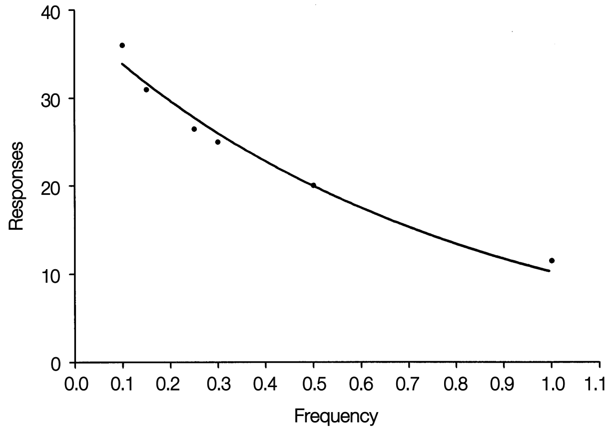

FIGURE 1: Relation between twitch stimulation rate and force response in the presence of d-tubocurarine. The response decreases exponentially as the stimulation rate increases from 0.1 to 1 Hz R^2=0.975. (Data from Figures 26-28, Monitoring of Neuromuscular Function. Ali HH, Miller RD, In: Anesthesia, ed. RD Miller, 2nd Ed. Churchill Livingstone, New York 1986; p. 883.)

noticeably. Tetanic stimulation has, therefore, often been used for detecting residual blockade visually or by feel. The test is readily applicable to the orbicularis oculi (or the corrugator supercilii) as well as the AP or other limb muscles. It has, however, been demonstrated that only high degrees of tetanic fade can reliably be detected by clinical means[55].

Tetanic stimulation at 50 Hz stresses neuromuscular transmission about as much as maximal voluntary effort[56]. Maintenance of tetanic contraction at 30 Hz stimulation requires only 20 to 25% of free receptors (at least in the cat tibialis anterior), about the same as 100% twitch response and similar to a TOF ratio of 0.7. To maintain the response at 100 Hz requires that about 50% of the receptors be available and at 200 Hz, about 67%[57]. It seems, therefore that 50 Hz is a reasonable choice for clinical testing.

The accumulation of acetylcholine during tetanic stimulation displaces competitive NMBD. Following tetanic stimulation and a short recovery interval, evoked acetylcholine release is also increased and therefore if single twitch stimulation is applied after a tetanic stimulus, the twitch response is enhanced. This is post-tetanic facilitation (PTF, Figure 2), which is usually detectable in normal subjects but in the presence of competitive NMB, especially when twitch is less than 30% of control, it becomes marked[58]. While it is often quite noticeable by inspection or palpation, it is unlikely to add discrimination to the presence or absence of tetanic fade in the detection of NMB, visually or by feel.

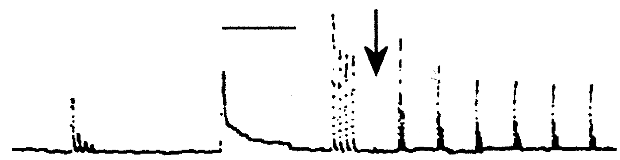

FIGURE 2: Post-tetanic facilitation. At the bar, a 5 s tetanic stimulus was applied. The amplitude of the T1 response is increased by a factor of 2.5, and there is a marked increase in TOF ratio. At the arrow, recording speed was reduced. (From reference 58, with permission.)

Train-of-four stimulation

Train-of-four stimulation pattern was described by Ali, Utting and Grey[59-61] and has become the most common pattern for clinical assessment or for measurement of NMB. It consists of a train-of-four square wave stimuli of 0.2 ms duration, at 0.5 Hz applied at 12 s intervals. Because in the presence of competitive NMB the response fades at this stimulation rate, the ratio of the amplitude of the response to the fourth. stimulus to that of the first, gives an indication of the intensity of the NMB. With onset of more profound NMB, the number of detectable responses is reduced from progressively from four to none (TOF count). As discussed above, good surgical conditions are compatible with the presence of one response. Rapid reversal usually follows the presence of two responses and good recovery from NMB requires a TOF ratio >0.9. The important advantage of the pattern is that a pre-NMB control recording is not needed to assess the presence or severity of NMB.

The disadvantage of the pattern is chiefly the difficulty of precisely estimating the ratio in the absence of a recording device.

To obtain maximal response at the AP, usually a current of about 40-50 mA is required[62]. To ensure the maintenance of maximal response, somewhat greater current, 50 to 60 mA is usually used. This is quite painful for awake patients, albeit not nearly as unpleasant as tetanic stimulation.

While it is common practice to use supramaximal stimulation, such high currents are quite painful. It has therefore been suggested that the use of submaximal current may not change the T4/T1 ratio and will therefore result in acceptable tests[63]. It has since been shown that while the mean of the responses with submaximal current correlate well with supramaximal control responses, the scatter increases to what may be an unacceptable level[64]. Both these studies used MMG measurement of the responses. Recently Brull reported that submaximal current enhanced the accuracy of visual and tactile assessment (S. J. Brull. Use of submaximal stimulation. 7th International Neuromuscular Meeting. Belfast, June 2001). The subject of submaximal stimulation current needs further work. For research, there is general agreement that supramaximal currents should be used, but there may be a place for submaximal current stimulation in the clinical environment, for reducing the incidence of postoperative NMB.

Neither here nor in the section on tetanic stimulation was the problem of persistent depolarizing block addressed. Such block may show neither tetanic fade nor significant reduction in the TOF ratio and for accurate evaluation, has to be compared to a pre-NMB control.

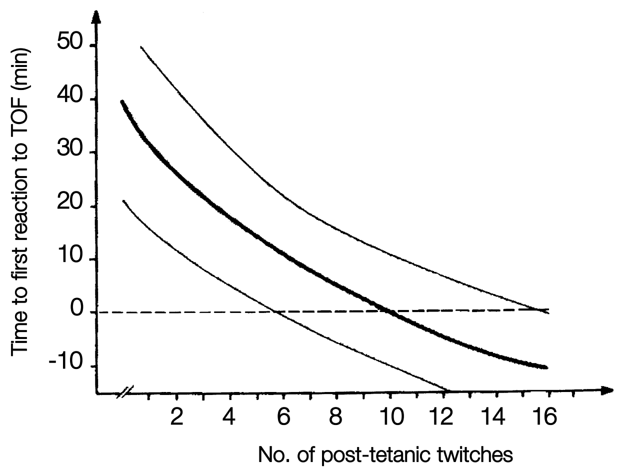

FIGURE 3: Relation between post-tetanic count and return of TOF response in the presence of pancuromium. The hatched region is the 95% confidence interval. (From reference 48, with permission.)

Double-burst stimulation

The double-burst stimulation pattern was developed in response to the obvious difficulty of visual and tactile evaluation of NMB with train-of-four stimulation pattern[29]. Four patterns were investigated and the chosen pattern, DBS(3,3) 50:50 consisted of 3, 0.2 ms stimuli at 50 Hz (20 ms intervals) followed 750 ms later by three more. This was shown to be more sensitive for manual detection of NMB than TOF stimulation. Later studies however have shown that while it reduced the incidence of postoperative residual blockade, it failed to eliminate the problem[14]. DBS has been evaluated with submaximal current[65-66] but appears to yield too many false positives, defined in the second study as apparent fade when the TOF ratio was >0.7. A number of modifications to the basic pattern have been proposed with changes in the number, frequency and duration of the pulses[67]. The use of an initial train-of-three stimuli followed by two stimuli, DBS (3,2), may bias the observer towards "feeling" fade and thereby reduce the incidence of residual blockade. DBS (3,3) 80:40 was suggested to monitor more profound NMB[68] as it evokes a response before the return of TOF twitches.

Post-tetanic count

Intense NMB cannot be quantified by twitch or TOF stimulation. Even before there is a return of a response to TOF, some quantitation of the NMB can be made by exploiting the PTF phenomenon. The post-tetanic count (PTC) is elicited by administering a 5 s, 50 Hz tetanic train, followed after a 3 s pause by twitches at 1 Hz[69]. A count of 10 or 11 twitches coincides usually with the reappearance of the first response to TOF stimulation. This can be used to maintain intense NMB but of course, it is not useful in predicting reversability of theNMB or the absence of residual blockade.

Post-tetanic burst

A combination of the post-tetanic count with double-burst has been described, which detects a response even before the PTC does. A 5 s, 50 Hz tetanus is followed after 3 s by trains of 3, 50 Hz impulses at 1 s intervals, instead of single twitches[70,71].

TABLE 2
Preferred patterns of stimulation for monitoring specific objectives

Pattern	Onset	Deep Block	Normal Block	Reversa-bility	Recovery
TOF*	+++*	0	+++	+++	++*
DBS**	0	+	++	++	++*
Tetanus	+	++	++	0	0
Post-tetanic count**	0	+++	0	0	0
Post-tetanic burst	0	+++	0	0	0

*Accuracy much improved by objective measurement.
**Evaluated at the thumb or corrugator supercilii.

WHICH MUSCLE TO MONITOR?

Possibly the most obvious practical consideration is the accessibility of the monitored muscle for observation during surgery. This is especially the case, where touch or sight is used for evaluation. Where measurements are made, this becomes less of a factor. With MMG and a force-displacement transducer, the thumb (or other extremity, such as toe) must be fixed and free of mechanical interference but using a "dynamic" piezoelectric transducer, EMG or accelerometry, the problems of access are much reduced. With EMG measurement, immobilization of the limb as with a light splint under the surgical drapes is sufficient. Change in the limb's position, however, may alter the EMG. Using a dynamic transducer or accelerometry, again, immobilization of the limb, with free movement of the thumb, toe or wherever the transducer is attached, is needed. A change in the position of the limb, for example some rotation, may change the direction of gravity and the resting stretch of the monitored muscle and hence the response in comparison with control value. The TOF ratio may not change. Obtaining stable conditions for recording the piezoelectric MMG, EMG or accelerogram under drapes is usually not difficult. Other important considerations come into play in the choice of site when the objectives of monitoring are considered. If it is the prevention of residual NMB, a sensitive muscle with slow recovery such as the AP is probably ideal. If the prime objective is the avoidance of any movement during operation, a less sensitive muscle, such as the gastrocnemius, flexor hallucis brevis or the corrugator supercilii may be preferred.

The adductor pollicis

Historically, the AP has been the muscle most frequently used for MMG monitoring and research measurements in humans. It has also traditionally been used for assessment by inspection or palpation. The piezoelectric transducers on commercially available systems also appear to be designed for use on the thumb. This muscle is also convenient for EMG recording, but the abductor digiti minimi is probably the muscle of choice in the hand for this.

The onset of paralysis at the AP is slower than at the larynx or the diaphragm as is recovery[72] and it is more sensitive to NMBD than laryngeal adductors[73] or the diaphragm, making it a poor choice as an indicator of onset of laryngeal blockade or avoidance of "bucking" but suitable for the detection of persistent postoperative blockade.

The abductor digiti minimi

This is the muscle most frequently used for EMG recording in the hand. The suggested positions for skin electrode placement for the recording electrodes, is the ulnar aspect of the dominant hand about one third distance from the distal carpal crease to the metacarpo-phalangeal crease and at the base of the little finger. The stimulating electrodes on the volar aspect of the forearm, over the ulnar nerve about 5 cm apart with negative distal. The ground or indifferent electrode is sited between the stimulating and recording electrodes[74].

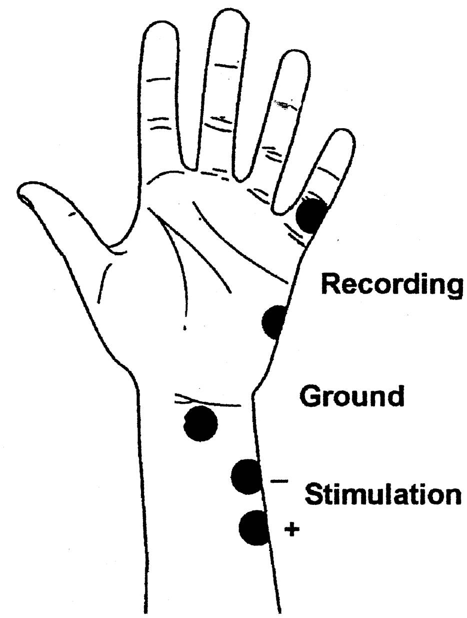

FIGURE 4: Suggested electrode placement for EMG monitoring of the abductor digiti minimi. (Re-drawn after reference 63.)

The gastrocnemius

Where a muscle of the leg is the most convenient monitoring location, the gastrocnemius has been suggested for EMG[75]. When compared to the AP, onset times were similar but the gastrocnemius recovered significantly more rapidly after vecuronium. In the writer's experience, supramaximal stimulation of the popliteal nerve as used in this study, caused quite significant leg movement, which may be distracting to the surgeon.

The flexor hallucis brevis

This muscle is also suitable for monitoring by MMG[76] or accelerography[77,78]. Stimulation can be applied to the posterior tibial nerve behind he medial malleolus. The characteristics of onset are not significantly different from the AP but recovery is more rapid at the toe.

The orbicularis oculi

The contraction of the orbicularis oculi evoked by stimulation of the facial nerve is usually easy to observe during surgery. It is therefore frequently used for visual monitoring but measurement of the response is possible by EMG or accelerometry (at least in some subjects)[79]. This muscle is less sensitive to NMBD than the AP and possibly even the diaphragm[64]. Onset of the blockade is quicker than in the AP and seems to parallel that at the larynx[80,81]. Recovery of the orbicularis oculi is slower than that of the laryngeal adductor muscles[65].

The corrugator supercilii

It has been suggested recently that what was the activity observed at the eyebrow in response to facial nerve stimulation was not principally that of the orbicularis oculi but due to the corrugator supercilii fibres of the periocular muscle[82]. In this recent paper, the authors demonstrate that this muscle parallels closely the laryngeal adductor muscles in onset, sensitivity and duration of NMB.

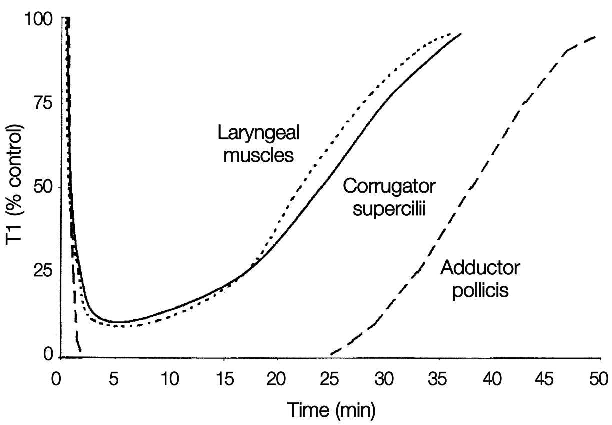

FIGURE 5: Relationship between paralysis in the laryngeal adductors, the corrugator supercilii and the adductor pollicis. The two former muscles are more resistant and recover more rapidly than the adductor pollicis. (From reference 66.)

The evoked responses of other muscles such as the adductors of the larynx or the diaphragm can be recorded for research purposes[60,61].

CONCLUSIONS

A number of points of interest emerge from reviewing the literature on neuromuscular monitoring. The first, which has already been discussed, concerns the choice of muscle to monitor. There is no single best monitoring site. The AP is indeed suitable, when the objective is to ensure ready reversal and to avoid residual NMB, but if the objective is to ensure motionlessness, a more resistant muscle may be a better choice. The corrugator supercilii would answer this requirement, were it not often too near the surgical field.

There is a significant incidence of residual NMB in the recovery room, even following routine reversal of the blockade. Bevan[22] makes the point that reversal should be routine, unless absence of NMB is actively demonstrated. This would have special implications for users of mivacurium. Adverse effects from persistent NMB are now well documented. Residual NMB is reduced by the use of a nerve stimulator in the operating room and the use of intermediate acting NMBD but the problem is not eliminated without objective and accurate measurement of blockade. Accelerometry appears to be the measuring modality of choice for clinical use. Relatively inexpensive accelerometers are now available so that, say, the cost of two extra inpatient days because of pulmonary complications due to residual NMB would more than cover the cost of an instrument. To introduce their general use, together with appropriate education seems, to the writer, to be overdue.

It seems also clear that the use of long-acting NMBDs results in increased incidence of residual paralysis[24,83]. Even if accurate monitoring is used, long-acting NMBDs are more likely to result in delays at the end of operations than if intermediate-acting drugs are used. It would therefore be reasonable to question their use.

The introduction of routine neuromuscular monitoring, preferably by measurement, will also pay dividends in smooth anaesthesia and when correctly used, the rapid conclusion of anaesthetics because of reduction in recovery times from NMB.

It is the writer's opinion that "... the proper use and interpretation of neuromuscular monitoring is a must" (Donati[84], 1998). At the recent International Neuromuscular Meeting (Belfast, June 2001) the recommendation for the universal use of nerve stimulators whenever NMBDs are administered was universally agreed and there was strong expressed preference for objective measurement of relaxation to avoid postoperative residual NMBs. As safety of anaesthesia improves, further gains will be incremental and the introduction of routine measurement of NMB offers an opportunity for reducing adverse events.

TABLE 3

Suitability of muscles as they affect neuromuscular monitoring

Muscle	Onset	Deep Block	Normal Block	Reversability	Recovery
Adductor pollicis	+	0	++	+++	+++
Abductor dig. min.*	+	0	++	+++	+++
Gastrocnemius**	+	+	+	++	++
Flex. hal. brevis	+	+	++	++	++
Corr. supercilii	+++	++	++	++	+

*For EMG.
**Causes severe leg movement.

REFERENCES

1. Lunn JN, Hunter AR, Scott DB. Anaesthesia related surgical mortality. Anaesthesia 1983; 38:1090-1096.
2. Tiret I, Desmonts LM, Hatton F, Vourch G. Complications associated with anaesthesia—a prospective study in France. Can J Anaesth 1986; 33:336-344.
3. Holland R. The New South Wales Survey. Brit J Anaesth 1987; 59:834-841.
4. Shorten GD. Postoperative residual curarisation: incidence, aetiology and associated morbidity. Anaesth Intensive Care 1993; 21:782-789.
5. Viby-Mogensen J, Viby-Mogensen B, Ording H. Residual curarization in the recovery room. Anesthesiology 1979; 539-541.
6. Fawcett WJ, Dash A, Francis GA Liban JB, Cashman JN. Recovery from neuromuscular blockade: residual curarisation following atracurium or vecuronium by bolus or dosing infusions. Acta Anaesthesiol Scand 1995; 39:288-293.
7. Hotton P, Burchett KR, Madden AP. Comparison of recovery after neuromuscular blockade by atracurium or pancuronium. Br J Anaesth 1988; 60:36-42.
8. Katz RL. Neuromuscular effects of d-tubocurarine, edrophonium and neostigmine. Anaesthesiology 1967; 28:327-336.
9. Koscielniak ZJ, Horn A, Sztuk F, Eriksen K, Theil Skovgaard L, Viby-Mogensen J. Timing of tracheal intubation: Monitoring the orbicularis oculi, the adductor pollicis or use a stopwatch? Eur J Anaesthesiol 1996; 13:130-135.
10. Booij LHDJ. Active reversal and monitoring of neuromuscular blockade. In Neuromuscular transmission Ed. Leo HDJ Booij, BMJ Publishing Group, London, 1996, p.170.
11. Booij LHDJ. Active reversal and monitoring of neuromuscular blockade. In Neuromuscular transmission Ed. Leo HDJ Booij, BMJ Publishing Group, London, 1996, p.169.
12. Katz RL. Clinical neuromuscular pharmacology of pancuronium. Anesthesiology 1971:34:550-556.
13. Beemer GH, Rozenthal P. Postoperative neuromuscular function. Anaesth Int Care 1986; 14:41-45.
14. Fezing AK, d'Hollander A, Boogaerts JG. Assessment of the postoperative residual curarization using the train of four stimulation with acceleromyography. Acta Anaesthesiol Belgica 1999; 50:83-86.
15. Shorten GD, Merk H, Sieber T. Perioperative train-of-four monitoring and residual curarization. Can J Anaesth 1995; 42:711-715.
16. Fruergaard K, Viby-Mogensen J, Berg H, El-Mahdi 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; 42:1169-1174.
17. Ali HH, Wilson RS, Savarese JJ, Kitz RJ. The effect of curare on indirectly elicited train of four muscle response and respiratory measurement in humans. Br J Anaesth 1975; 47:570-574.
18. Brand JB, Cullen DJ, Wilson NE, Ali HH. Spontaneous recovery from non-depolarizing neuromuscular blockade: Correlation between clinical and evoked responses. Anesth Analg 1977; 56:55-58.
19. Pavlin EG, Holle RH, Schoene RB. Recovery of airway protection compared with ventilation in humans after paralysis with curare. Anaesthesiology 1989; 70:381-385.
20. Engbaek J, Ostergaard D, Viby-mogensen J, Skovgaard LT. Clinical recovery and train-of-four measured mechanically and electromyographically following atracurium. Anesthesiology 1989; 71:391-395.
21. Bevan DR, Neuromuscular Monitoring after surgery. Can J Anaesth 1990; 37:395-396.
22. Eriksson LI, Sundman E, Olsson R, Nilsson L, Witt H, Ekberg O, Kuylenstierna R. Functional assessment of the pharynx at rest and during swallowing in partially paralysed persons: Simultaneous videomanometry and mechanomyography in awake human volunteers. Anesthesiology 1997; 87:1035-1043.
23. Eriksson LI, Sato M, Severinghaus JW. Effect of a vecuronium-induced partial neuromuscular block on hypoxic ventilatory response. Anesthesiology 1993; 78:693-699.
24. Berg H, Viby-Mogensen J, Roed J et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications: A prospective randomised and blinded study of postoperative complications after atracurium, vecuronium and pancuronium. Acta Anaesthesiol Scand 1997; 41:1095-1103.
25. Viby-Mogensen J. Postoperative residual curarization and evidence based anaesthesia. Brit J Anaesth 2000; 84:301-303.
26. Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. Anesthesiology 1977; 86:765-771.
27. Pedersen T, Viby-Mogensen J, Bang U, Olsen NV, Jensen E, Engbaek J. Does perioperative tactile evaluation of the train-of-four response influence the frequency of postoperative residual neuromuscular blockade? Anesthesiology 1990; 73:835-839.
28. Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chaemmer-Jorgensen B. Tactile or visual evaluation of response to train-of-four nerve stimulation. Anesthesiology 1985; 63:440-443.
29. Saddler JM, Bevan JC, Donati F, Bevan DR, Pinto MB. Comparison of double-burst and train-of-four stimulation to assess neuromuscular blockade in children. Anesthesiology 1990; 73:401-403.
30. 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.
31. Churchill-Davidson HC, Christie TH. Diagnosis of neuromuscular block in man. Brit J Anaesth 1959; 31:290-295.
32. Engbaek J, Skovgaard IT, Friis B,Kann T, Viby-Mogensen J. Monitoring of the neuromuscular transmission by electromyography. (I) Stability and temperature dependence of the evoked EMG response compared to mechanical twitch recording in the cat. Acta Anaesthesiol Scand 1992; 36:495-504.
33. Epstein RA, Epstein RM. The electromyogram and the mechanical response of indirectly stimulated muscle in anesthetized man following curarization. Anesthesiology 1973; 38:212.
34. Comparison of electrical and mechanical recording of spontaneous and evoked muscle activity. Anesthesiology 1965; 26:204.
35. Katz RL. Electomyographic and mechanical effects of suxamethonium and tubocurarine on twitch, tetanic and post-tetanic responses. Br J Anaesth 1973; 45:849.
36. Kopman AF. The effect of resting muscle tension on the dose-effect relationship of d-tubocurarine: does preload influence the evoked EMG. Anesthesiology 1988; 69:1003-1005.
37. Donlon JV, Savarese JJ, Ali HH. Cumulative dose-response curves for gallamine:effect of altered thumb tension and mode of stimulation. Anesth Analg 1979; 28:337-381.
38. Viby-Mogensen J, Engbaek J, Eriksson LI, Gramstad L, Jensen E, Jensen FS, Koscielnak-Nielsen Z, Skovgaard LT,

Ostergaard D. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents. Acta Anaesthesiol Scand 1996; 40:59-74.
39. Shanks C. Harrison GA. Mechanical factors affecting the evoked pressures from a simple twitch monitor. Anaesth Intensive Care 1972; 1:154-156.
40. Newell S. Brimacombe J. A homemade device for monitoring neuromuscular blockade. Anaesth Intensive Care 1995; 23:522-523.
41. Newell S. Brimacombe J. Measurement of neuromuscular blockade—a comparison between a new "homemade" force displacement transducer and the accelerometer. Anaesth Intensive Care 1995; 23:203-205.
42. Pohlen G, Ribeiro FC, Schreiber G. Plethysmechanomyography (PMG). A simple method for monitoring relaxation. Anaesthetist 1994; 43:773-779.
43. Torda TA. A force-displacement transducer for quantitation of neuromuscular block. Anaesth Intensive Care 1972;1:157-158.
44. Kirkegaard-Nielsen H, Helbo-Hansen HS, Pedersen HS, Severinsen IK, Schmidt MB. New equipment for neuromuscular transmission monitoring: A comparison of the TOF-Guard with the Myograph 2000. J Clin Monitoring & Computing 1998; 14:19-27.
45. Dahaba AA, Rehak PH, List WF. Assessment of accelerography with the TOF-Guard: A comparison with electromyography. Europ J Anaesthesiol 1997; 14:623-629.
46. Mortensen CR, Berg H, El-Mahdy A, Viby-Mogensen J. Perioperative monitoring of neuromuscular transmission using accelerography prevents residual neuromuscular block following pancuronium. Acta Anaesthesiol Scand 1955; 39:797-801.
47. Kern SE, Johnson JO, Westenskow DR, Orr JA. A comparison of dynamic and isometric force sensors for train-of-four measurement using submaximal stimulation current. Journal of Clinical Monitoring 1995; 11:18-22.
48. Dahaba AA, v Klobucar F, Rehak PH, List WF. Comparison of a new piezoelectric train-of-four neuromuscular monitor, the ParaGraph, and the Relaxometer mechanomyograph. Br J Anaesth 1999; 82:780-782.
49. Dascalu A, Geller E, Moalem Y, Manoah M, Enav S, Rudick Z. Acoustic monitoring of intraoperative neuromuscular block. Br J Anaesth 1999; 83:405-409.
50. Katz RL. A nerve stimulator for the continuous monitoring of muscle relaxant action. Anesthesiology 1965; 26:832.
51. Heisterkamp DV, Cohen PJ. Technical note concerning the Bloc-Aid monitor. Anesthesiology 1968; 29:1210-1211.
52. Iwasaki H, Igarashi M, Namiki A. A preliminary clinical evaluation of magnetic stimulation of the ulnar nerve for monitoring neuromuscular transmission. Anaesthesia 1994; 49:814-816.
53. Viby-Mogensen J. Clinical assessment of neuromuscular transmission. Br J Anaesth 1982; 54:209-223.
54. Ali HH, Savarese JJ. Monitoring of neuromuscular function. Anesthesiology 1976; 45:216-221.
55. Dupuis JY, Martin R, Tessonier JM, Tetrault JP. Clinical assessment of the muscle response to tetanic nerve stimulation. Can J Anaesth 1990; 37:397-400.
56. Merton PA. Voluntary strength and fatigue. J Physiol 1954; 123:553.
57. Waud BE, Waud DR. The relation between tetanic fade and receptor occlusion in the presence of competitive neuromuscular block. Anaesthesiology 1971; 35:456-464.
58. Torda TA, Graham GG, Tsui D. Neuromuscular sensitivity to atracurium in humans. Anaesth Intensive Care 1990; 18:62-68.
59. Ali HH, Utting JE, Grey C. Stimulus frequency and the detection of neuromuscular block in humans. Br J Anaesth 1970; 42:967.
60. Ali HH, Utting JE, Grey C. Quantitative assessment of residual antidepolarizing block (part I). Br J Anaesth 1971; 43:473-477.
61. Ali HH, Utting JE, Grey C. Quantitative assessment of residual antidepolarizing block (part II). Br J Anaesth 1971; 43:478-482.
62. Kopman AF Lawson D. Milliamperage requirement for supramaximal stimulation of the ulnar nerve with surface electrodes. Anaesthesiology 1984; 61:83-85.
63. Brull SJ, Ehrenwerth J, Silverman DG. Stimulation with submaximal current for train-of-four monitoring. Anesthesiology 1990; 72:629-632.
64. Helbo-Hansen HS, Bang U, Kierkegaard Nielsen H, Skovgaard LT. The accuracy of train-of-four monitoring with submaximal currents. Anaesthesiology 1992; 76:199-203.
65. Silverman DG, Brull SJ. Assessment of double burst monitoring at 10 mA above threshold current. Can J Anaesth 1993; 40:502-506.
66. Saitoh Y, Fujii Y, Makita K, Tanaka H, Amaha K. Modified double burst stimulation of varying stimulating currents. Acta Anaesthesiol Scand 1998; 427:851-857.
67. Kierkegaard-Nielsen H, May O. The influence of double burst stimulation (DBS) pattern on the DBS-train-of-four ratio relationship. Anesthesiologie, Intensivemedizin, Notfallmedizin, Schmetztherapie 1995; 30:163-166.
68. Kierkegaard-Nielsen H, Helbo-Hansen HS, Severinsen IK, Lindholm P, Bulow K. Acta Anaesth Scand 1996; 40:719-723.
69. Viby-Mogensen J, Howardy-Hansen P, Chraemmer-jorgensen E, Ording H, Engbaek J, Nielsen A. Post-tetanic count (PTC). Anew method of evaluating an intense non-depolarizing neuromuscular blockade. Anesthesiology 1981; 55:458-462.
70. Saitoh Y, Toyooka H, Amaha K. Post-tetanic burst: a new monitoring method for intense neuromuscular block. Brit J Anaesth 1995; 74:293-295.
71. Saitoh Y, Fuji Y, Toyooka H, Amaha K. Post-tetanic burst count: a stimulating pattern for profound neuromuscular blockade. Can J Anaesth 1995; 42:1096-1100.
72. Donati F, Meistelman C, Plaud B. Vecuronium neuromuscular blockade at the diaphragm, the orbicularis oculi, and adductor pollicis muscles. Anesthesiology 1990; 73:870-875.
73. Meistelman C, Plaud B, Donati F. Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. Can J Anaesth 1992; 39:665-669.
74. Smans J, Korsten HHM, Blom JA. Optimal surface electrode positioningfor reliable train of four muscle relaxation monitoring. Int J Clin Monitoring and Computing 1996; 13:9-20.
75. Saitoh Y, Narmi Y, Fuji Y, Ueki M, Makita M. Electromyographic assessment of neuromuscular block at the gastrocnemius muscle. Br J Anaesth 1999; 82: 329-332.
76. Saitoh Y, Fuji Y, Takahashi K, Makita K, Tanaka H, Yamaha K. Recovery of post-tetanic count and train-of-four responses at the great toe and thumb. Anaesthesia 1998; 53:244-248.
77. Kitajima T, Ishii K, Ogata H. Assessment of neuromuscular block at the thumb and great toe using accelerography in infants. Anaesthesia 1996; 51:341-343.
78. 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; 43:550-555.
79. Caffrey RR, Warren MI, Becker KE Jr. Neuromuscular blockade monitoring comparing the orbicularis oculi and the adductor pollicis muscles. Anesthesiology 1986; 65:95-97.

80. Ugureanu D, Meistelman C, Frossard J, Donati C. The orbicularis oculi and the adductor pollicis muscles as monitors of atracurium block of laryngeal muscles. Anesth Analg 1993; 77:775-779.
81. DebaeneB, Beaussier M, Meistelman C, Donati F, Lienhart A. Monitoring the onset of neuromuscular block at the orbicularis oculi can predict good intubating conditions during atracurium-induced neuromuscular block. Anesth Analg 1995; 80:360-363.
82. 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.
83. Bevan DR, Smith CE, Donati F. Postoperative neuromuscular blockade: a comparison between atracurium, vecuronium and pancuronium. Can J Anaesth 1988; 69:272-276.
84. Donati F. Neuromuscular monitoring: useless, optional or mandatory? Can J Anaesth 1998; 45:R106-R111.