Continuing Medical Education Article

Clinical use of peripheral nerve stimulators in anaesthesia

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Contents

Introduction

Neuromuscular blockade facilitates tracheal intubation and provides the muscle relaxation essential to certain operations. Assessment of neuromuscular blockade rested solely on clinical observations in the past but is now often assisted by data obtained from use of peripheral nerve stimulators.

Churchill-Davidson outlined the rationale for the use of a peripheral nerve stimulator (PNS).[1] First, monitoring neuromuscular blockade helps the anaesthetist use the correct dose of relaxant. Many clinical signs of neuromuscular recovery, such as the ability to lift the head, respiratory parameters (vital capacity and tidal volume), sustained hand squeeze and eye opening cannot be elicited during the course of anaesthesia. However, information can be obtained with a PNS, which minimizes the risks of prolonged paralysis in the postoperative period. Second, at the end of an operation use of a PNS allows the dose of anticholinesterase to be adjusted to the patient's needs. Third, Phase II block can be identified with the aid of a PNS, as the twitch response would change from that of a depolarizing to a non-depolarizing block.

Although many publications express neuromuscular blockade in terms of precise measurement of the height of twitches (Figure 1), the popularity and potential of using a PNS in the clinical setting lies in the fact that useful information can be obtained by observing patient's response to stimuli with the use of inexpensive equipment (costing about Can $500). However, to obtain accurate information the measuring system must satisfy the criteria that for each twitch, the nerve is supramaximally stimulated only once by the stimulus, all the muscle fibres depolarize once and only once in response to such a stimulus, and the contractile force is indeed an index of the proportion of the fibres depolarized. The conditions which affect measurement of neuromuscular blockade are: the machine characteristics, the machine-patient-interface and patient conditions (Table I). The use of muscle relaxants has been discussed in a previous article in the *Continuing Medical Education Section* of the Journal.[2] Patient conditions affecting neuromuscular blockade, such as temperature, acid–base balance and electrolytes, have been discussed elsewhere.[3,4] This article confines itself to a review of those conditions pertaining to stimulator characteristics and the stimulator-patient interface. Peripheral nerve stimulators can also be used to locate nerves for regional blockade but discussion of this topic is beyond the scope of this article.

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It is necessary to understand some basic terms which are used in the subsequent discussions. *Single twitch height* is a measurement of the force (e.g., from movement of a thumb) resulting from a single stimulus of the motor nerve innervating the muscle. Figure 1 shows single twitch heights which decrease with the onset of neuromuscular blockade and recover as the blockade decreases. *Train-of-four* are twitch height responses to four consecutive stimuli, each 0.5 seconds apart. The train-of-four pattern from a depolarizing block differs from a non-depolarizing block (Figure 2). *Tetanus* is obtained by the stimulation of a nerve with frequencies exceeding 50 per second, which simulates physiologic conditions of firing at the neuromuscular junction.

Machine characteristics

Stimulus frequency

When applying single twitch, train-of-four or tetanic stimuli to a nerve, the stimulus frequency affects the response. In studying the single twitch stimulation of the ulnar nerve, it was found that stimuli applied more often than 0.1 to 0.15 hertz (Hz) were associated with a progressively diminished response.[5,6] This observation is probably attributable to the depletion of acetylcholine at the nerve terminal. Thus, stimuli applied more often than 0.1 Hz will result in overestimation of the degree of neuromuscular blockade. Sustained muscle tension to tetanic stimulation will become nonsustained and will fade at higher frequencies.[7] These higher frequencies exceed 50 Hz, the frequency necessary for stressing the neuromuscular junction, to the same degree as a maximal voluntary effort.[8] Thus, as the stimulus frequency is increased, blockade appears to be more pronounced. In fact, at high enough frequencies tetanic fade will appear even in the absence of any neuromuscular blocking agents. This fade occurs earlier at higher frequencies. For example, fade occurs in two seconds at 150 Hz and in one second at 300 Hz.[9]

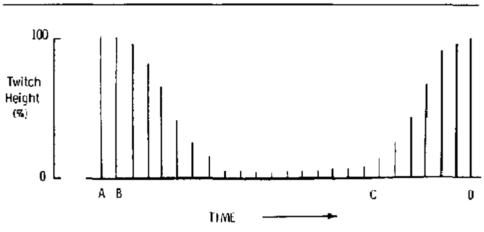

FIGURE 1 Schematic diagram illustrating the changes in the twitch height with PNS in a patient who has received neuromuscular blocking drug. (A) Before receiving drug. (B) Drug given; twitch height diminishes after this. (C) As drug wears off, twitch height starts to recover. (D) Twitch height has fully recovered.

TABLE 1 Conditions which affect the interpretation of responses to peripheral nerve stimulation

Machine characteristics
stimulus frequency
wave-form
wave-width
current
voltage
Machine-patient-interface
type of electrode
site of stimulation
polarity of electrode
methods for the scoring of the response
Patient conditions
type of neuromuscular blocking drug used
acid base balance
electrolyte balance
core temperature
presence of anesthetic agents

To minimize overestimation of blockade, several authors have suggested "rules of thumb" to follow.[2,10-12] For example, tests for single twitch or train-of-four should not be repeated within an interval of ten seconds. Tetanic stimuli should be given at physiological levels of 30 to 50 Hz for five second durations and an interval of two minutes should be allowed before it is repeated.[2] This

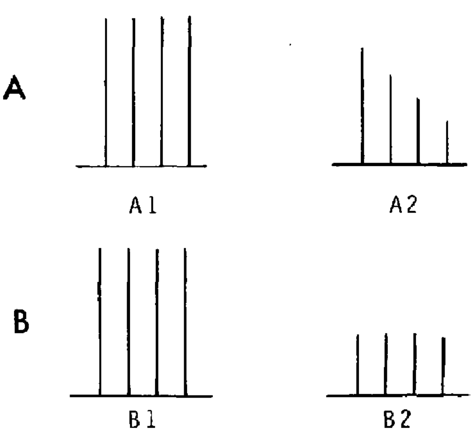

FIGURE 2 Schematic diagram illustrating the pattern of train-of-four with depolarizing and non-depolarizing blocks. (A1) Train-of-four before blockade. (A2) Train-of-four after non-depolarizing block has been established. There is progressive suppression of twitch height in all four twitches. (B1) Train-of-four before blockade. (B2) Train-of-four after depolarizing block has been established. There is equal suppression of twitch height with all four twitches.

allows the neuromuscular end-plate to return to a steady-state between stimuli.

Wave-form

Two major characteristics of the output wave-form from a PNS are its shape and duration. To avoid a tetanic-like stimulation and to minimize repetitive firing as would happen if the pulse is of longer duration than the muscle refractory period, the optimum single twitch is evoked with a 0.2 to 0.3 milliseconds single square wave electric pulse.[4,5,12–14] Non-square-wave pulses can cause repetitive firing of the nerve as was shown with the Block-Aid® monitor which gave dual pulses five milliseconds apart.[13] This pattern of stimulation can cause underestimation of the degree of block.

Requirement to evoke supramaximal stimulus (SMS)

The stimulus intensity must exceed what is necessary to achieve activation of all nerve fibres in the nerve tested; a condition called "supramaximal stimulation." This ensures that estimates of neuromuscular blockade are not in error due to failure to stimulate all the nerve fibres.

Although the idea of SMS is conceptually elegant, it is difficult to achieve. It is impossible to determine whether all nerve fibres are activated. Twitch tension measured at patients' wrists increased linearly with current load in the range of 15 to 30 milliamperes (mA).[15] However, there was no precise plateau where increased current did not increase twitch tension. The twitch tension continued to increase slowly, even at currents above 30 mA. The SMS chosen by the investigators was the current at the top of the steep linear portion of the slope of the twitch tension versus current curve. The results of this study also showed that, for wrist circumferences of less than 16 cm, 30 mA was sufficient to achieve SMS. However, for wrist circumferences of greater than 16 cm, currents of 30 mA to 50 mA were needed to achieve SMS. It was also suggested that the SMS was achieved with a current which is 2.75 times the current to evoke the minimal twitch in the thumb.

Since we will not know exactly the resistance of a subject, it is useful if a PNS contains an ammeter so that the current delivered can be displayed. In this way we can be sure that the appropriate current for SMS is being delivered. Such a display will also alert us to the possibility of a disconnection or poorly conducting electrode surfaces, as the current will then be reduced or absent.

TABLE II Placement of stimulating electrodes

Site of stimulation	*Monitor*	*References*	*Remarks*
WRIST			
Both electrodes at the wrist, one on ulnar nerve, the other on median nerve (Figure 3A)	Thumb adduction	33	
Both electrodes at the wrist along the ulnar nerve (Figure 3B)	Thumb adduction	12, 13, 24, 30, 31, 32	Adductor pollicis brevis is the only muscle supplied by the ulnar nerve to exert thumb adduction
Electrodes placed 2 cm and 9 cm from the ulnar head (Figure 3C)	Thumb adduction	29	
One electrode at the wrist, one at the olecranon (Figure 3D)	Thumb adduction	24, 33, 34	Ref. 33, 34 indicated that the active electrode is placed at the wrist
LEG			
Posterior tibial nerve (Figure 4A)	Plantar flexion of big toe	4, 30	
Peroneal nerve (Figure 4B)	Dorsiflexion of foot	4	
HEAD			
Temporal branch of the facial nerve (Figure 5A)	Frontalis muscle	12	
2 cm lateral to, 2 cm above and below the lateral canthus of the eye (Figure 5B)	Eyelids or supraorbital ridge	29	
One electrode between the mastoid process and the ear, another anterior to the ear (Figure 5C)	Orbicularis occuli	30	

Current and voltage requirements

The PNS should maintain constant current output, rather than constant voltage output since current is the determining factor for nerve stimulation.[16] In an attempt to keep the stimulus constant, most stimulators will vary their voltage with different resistances to deliver a constant current. Various PNS models have this useful capability (e.g., Bard Biomedical: Model 750; Biometer: Myotest).[17,18]

This feature has been tested in some PNS. At the extreme of high resistances there has been variability in the current produced. In fact, the current fell by up to 88 per cent at loads of 10,000 ohms in one model.[18,20] Many PNS will allow for the adjustment of voltage up to 300–400 volts or current from 25 to 70 mA.[20] In the clinical setting, resistances may change because of hypothermia and reduction of peripheral circulation. Only stimulators with features which maintain current constancy can assure continued SMS through the operation.

Machine-patient-interface

Type of electrode

The choice of electrodes includes needles, gel electrodes or spherical-ended probes or plates. The initial concern about burns caused by spherical-ended probes such as those provided with the Wellcome® PNS was later alleviated with the use of EKG type of pregelled electrodes.[19,21,22] These electrodes were easily applied, self-adhering, noninvasive and comfortable. They were used at the ulnar, peroneal and facial nerve sites and no burns were reported, although there were a few cases of erythema at electrode sites.[23,24]

Pregelled surface electrodes can potentially overestimate the neuromuscular block when a constant voltage PNS is used. The larger electrode surface area diminishes current strength, which makes delivery of an SMS less likely.[12,19] Proper preparation of the skin decreases resistance and increases the current delivered. This can be accomplished by scraping excess keratin from the skin and cleaning with alcohol, before electrode placement. Needle electrodes may be more useful for an obese patient or a patient with very cold extremities in whom resistance is likely to be high.[10,12] Although needle electrodes give the best contact, there are many objections to their use. Their placement in an awake patient causes discomfort. They have been associated with infection, broken needles and intraneural placement.

Site of stimulation

For obvious reasons, the site of measurement for neuromuscular blockade (e.g., an extremity) should be away from the surgical field (e.g., abdomen). The degree of neuromuscular blockade measured by testing a peripheral nerve may not adequately reflect the degree of blockade of the respiratory or abdominal muscles. It is well known that the respiratory muscles are less sensitive to neuromuscular blockade than the muscles of the extremities or those used for raising the head.[25–28] The implication of this is that neuromuscular recovery shown by testing peripheral nerves or head lift should ensure respiratory recovery.

There is also variation in the degree of sensitivity to blockade among different peripheral nerves. For example, periorbital stimulation tends to underestimate the block as compared to ulnar nerve stimulation.[29] This is due to either inability to achieve an SMS, differential muscle sensitivity or direct muscle stimulation which bypasses the neuromusular end-plate. With the same degree of blockade, and assessed by train-of-four, surface electrodes on the facial nerve will produce a better response than needle electrodes on the ulnar nerve which in turn will produce a better response than surface electrodes.[29]

There are several configurations for the placement of the electrodes. The ulnar nerve-adductor pollicis muscle system has been used most frequently because of its accessibility and resemblance to the standard laboratory single nerve muscle preparation. There are at least four ways suggested by investigators to stimulate the ulnar nerve (Figure 3).[12,13,24,29–34] The leg nerves which are easily accessible to the anaesthetist include the posterior tibial and the peroneal (Figure 4), which differ significantly in size. Their surrounding structures present different impedances to the nerve stimulator.[4,30] Since the facial nerve supplies all the facial muscles of expression,[35] more than one branch of the facial nerve is stimulated simultaneously. The various configurations for the placement of electrodes, the corresponding muscle to be monitored and the sources of reference are summarized in Table II. We prefer the placement of electrodes so that the monitoring site is most readily observed. If a hand is accessible (e.g., most abdominal, thoracic, and gynaecological cases), the ulnar nerve is used (Figure 3B). If the ulnar nerve is not accessible, and the anesthetist is near the patient's head, we prefer placing both electrodes at the lateral canthus of the eye for facial nerve stimulation (Figure 5B). However, at this time there is little information to allow for the correlation of the observations from one site to those obtained from another.

Polarity of electrode

The output from a nerve stimulator includes an anode (often colored RED) and a cathode (often colored BLACK). These two terminals from the output are attached to the electrodes on the patient. It has been appreciated in the past that after stimulation, a subsequent stimulation effected with the polarity reversed may

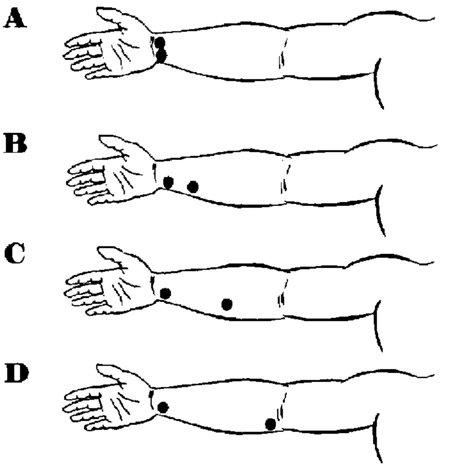

FIGURE 3 Various configurations of placement of electrodes to stimulate the ulnar nerve: both electrodes at the wrist, one on the ulnar nerve and the other on the median nerve (A); both electrodes at the wrist, along the ulnar nerve (B); electrodes placed 2 cm and 9 cm from the ulnar head (C); and one electrode at the wrist, the other at the olecranon (D).

sometimes increase the amplitude of the evoked response.[10] The electrode placed near the nerve concentrates the current on the nerve and is termed the active electrode. The other electrode which is placed further away and is used to complete the circuit is called the inactive or indifferent electrode. When the ulnar and median nerves were stimulated, it was found that if the active electrode is the cathode (negative), the responses to single twitch stimuli were greater.[33,34] However, polarity did not affect twitch height if the electrodes were placed within 5 cm of each other at the wrist.[34] This was presumably because the negative electrode was never so far from the nerve that it could not stimulate it. Increasing the distance of the electrode from the nerve reduces twitch height since the increase in resistance causes a decrease in current density and possible failure to produce a supramaximal stimulus. We recommend that the negative electrode be placed nearer to the nerve to be stimulated.

Scoring of the evoked responses

Results of stimulation can be assessed either visually, by tactile evaluation, measurement of mechanical tension or electromyographic measurements. Visual assessment of the train-of-four and the presence of fade at 50 Hz tetanic stimulation is possible.[36–38] However, it is not possible to quantitate the single twitch height to its control ratio or, in the case of train-of-four, the height of the fourth twitch to that of the first (the T4 ratio) without the use of a transducer. The general principle involves making measurements of tension during isometric contraction of a muscle group. One example is the adductor pollicis muscle in response to stimulation of the ulnar nerve. In this case, the thumb would act on a force-displacement transducer and tension would be converted to an electrical signal which can be presented on a paper strip. Using this approach, one can compare single twitch heights to a control or evaluate the T4 ratio.

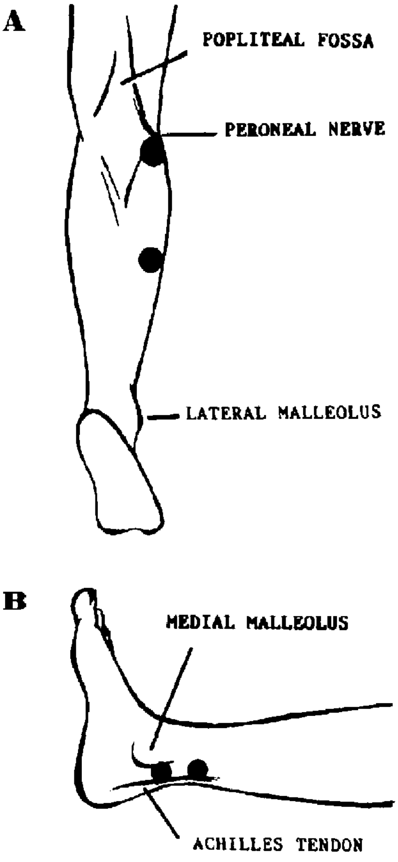

FIGURE 4 Various configurations of placement of electrodes on the leg: between the medial malleolus and the Achilles tendon (A); and on the peroneal nerve near the popliteal fossa (B).

During intense blockade, when the patient exhibits no visual response to single twitch, tetanic or train-of-four stimulation, placing one's hand on the patient's thumb during stimulation (tactile evaluation) can provide information regarding the patient's neuromuscular blockade.[32]

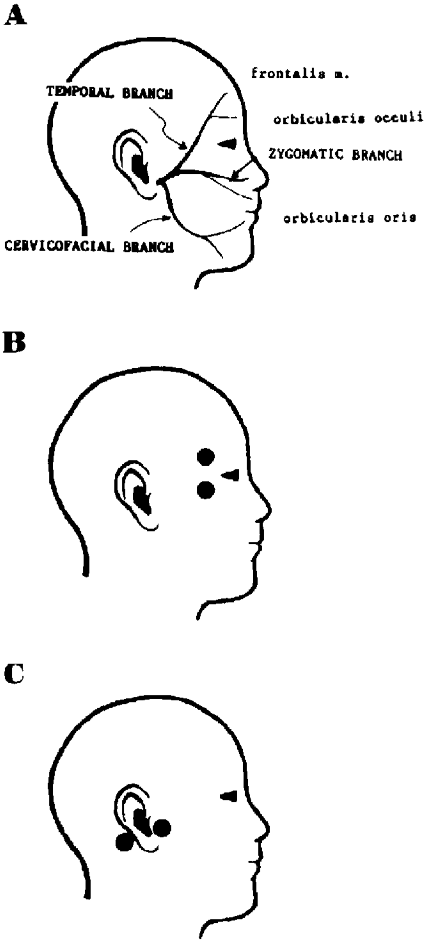

FIGURE 5 Various configurations of placement of electrodes to stimulate nerves on the face: along the temporal branch of the facial nerve (A); lateral to the canthus of the eye (B); and adjacent to the ear (c).

Interpretation of results

a. Tests performed in the monitoring of neuromuscular blockade

SINGLE TWITCH

This form of monitoring involves recording the strength of a control twitch and then comparing single twitch heights against the control. At twitch heights greater than 25 per cent of the control, abdominal muscles would still be tight. Surgical relaxation is usually provided by blockade to a twitch height of 5 to 25 per cent of control.[3,10] Even at a level of 75 per cent receptor occlusion, the twitch height remains 100 per cent of the control.[37] This demonstrates the neuromuscular safety factor ensured by receptor redundancy.

However, the use of twitch height alone may be misleading. At twitch heights of 90 per cent of control a patient will fail clinical tests and be unable to raise his head. With a twitch height of 100 per cent of control, which can be achieved in the face of 75 per cent receptor occupancy, residual curarization can still be shown with the train-of-four ratio and a tetanic stimulus at 50 Hz.[3,37,39]

TRAIN-OF-FOUR AND TRAIN-OF-FOUR RATIO

This method involves the delivery of four stimuli at 2 Hz. At this stimulus frequency transmitter depletion occurs and in patients with non-depolarizing block, progressive fade in twitch response is observed. This fade and loss of twitches in the train depend on the degree of block and can be quantitated visually. The train-of-four measurement is simple, does not involve elaborate equipment to measure the evoked responses and requires no control. The correlation of train-of-four to the degree of block is well established and can be found in all standard texts.[36,40,41] Briefly, during the onset of blockade, the fourth response is eliminated at 75 per cent block, the third at 80 per cent, and the second at 90 per cent.

The train-of-four ratio (T4 ratio) is defined as the amplitude of the fourth to the amplitude of the first twitch in a train-of-four, expressed as a percentage.[39] In conscious volunteers given d-tubocurarine a T4 ratio of greater than 70 per cent correlated with no change in respiratory rate, vital capacity, negative inspiratory force, tidal volume or peak expiratory flow rates. At levels of T4 ratio of 60 per cent there were reductions of negative inspiratory force and vital capacity.[42,43] In patients a T4 ratio of 74 ± 5 per cent correlates well with signs of clinical recovery from non-depolarizing neuromuscular block: eye opening, ability to protrude the tongue and cough, sustaining five seconds of head lift and a vital capacity of greater than 15–20 $\text{ml}\cdot\text{kg}^{-1}$. It also correlates with sustained tetanus at 30 to 50 Hz for five seconds.[7,39,43,44] At deeper levels of block during surgery when the T4 ratio is zero, a count of the number of twitches in the train will quantitate the block. The train-of-four should not be repeated more often than every 10 to 12 seconds to avoid effects of residual transmitter depletion.

TETANUS

The application of rapid stimuli for a period of time will cause acetylcholine depletion at the neuromuscular junction. The resulting failure of neuromuscular transmission from this depletion of transmitter will cause fade of response in the presence of non-depolarizing neuromuscular blocking agents. Tetanus may appear normal at low frequencies but fade at higher frequencies, thus unmasking residual curarization.[7,12,39,45] At 20–25 per cent receptor availability the tetanic response at 30 Hz for five seconds will be normal and will not fade. At 100 Hz for five seconds one needs 50 per cent of the receptor pool free to have no fade of response. At 200 Hz for five seconds one must have greater than two-thirds of the receptor pool free to avoid fade.[38] It has therefore, been advocated that 100 Hz tetanus should be used, to pick up residual curarization more easily. However, in most patients sustained tetanus of 50 Hz for five seconds correlates with 100 per cent single twitch height and with a train-of-four ratio greater than 0.7. A fade at 100 Hz tetanus was shown when the T4 ratio was as high as 0.88. If used alone, this will cause unnecessary or excessive use of anticholinesterase.[46] One must bear in mind that at high frequencies fade can occur without neuromuscular blocking drugs.[9] This is the reason why one should not try to assess residual blockade using frequencies higher than 100 Hz. Fifty hertz seemed to be the ideal stimulus frequency since it correlates well with maximal voluntary muscle effort.[8] In comparison with the single twitch, tetanic fade is more sensitive.[45] One disadvantage of tetanic stimulation is the discomfort it causes in the awake patient.

POST-TETANIC FACILITATION

The response to a tetanic stimulus and its resultant transmitter depletion increases synthesis and mobilization of acetylcholine. Stimuli applied six to ten seconds later will cause more transmitter release and result in a stronger twitch response. At very deep levels of neuromuscular blockade where train-of-four or single twitch are not helpful one can use post-tetanic facilitation to quantitate the block. It was shown that the number of post-tetanic twitch responses (post-tetanic count) could predict the time of return of the response to train-of-four stimuli.[32,47] The appearance of any post-tetanic twitch preceded the first return of the response of train-of-four by an average of 37 minutes.[47] Post-tetanic response can also be used as a diagnostic test to determine the type of neuromuscular block present.

b. Type of neuromuscular blockade

NON-DEPOLARIZING BLOCK

This type of neuromuscular blockade is caused by drugs which compete for the receptors with acetycholine at the muscle end plate without depolarizing it. Examples of these agents are d-tubocurarine, pancuronium, metocurine, atracurium, vecuronium and gallamine. Characteristics of this type of neuromuscular blockade include:[3,4,10]

(i) Absence of fasciculations prior to the blockade.
(ii) Nonsustained response to stimuli. Tetanic fade at fast rates and twitch height depression at slow rates.
(iii) Post-tetanic potentiation.
(iv) Antagonism of the block by anticholinesterases.
(v) Antagonism of the block by depolarizing muscle relaxants.
(vi) Potentiation of the blockade by other non-depolarizing drugs.

DEPOLARIZING BLOCK

This type of neuromuscular blockade is produced by drugs which cause the end plate of the neuromuscular junction to be depolarized. It is seen with succinylcholine and decamethonium and is characterized by:[3,4,10]

(i) Muscle fasciculation prior to onset of the block.
(ii) Initial absence of fade at slow and fast rates of stimulation.
(iii) No post-tetanic potentiation.
(iv) Potentiation of the block by anticholinesterases.
(v) Antagonism of the block by non-depolarizing relaxants.
(vi) Potentiation of the block by other depolarizing relaxants.

PHASE II BLOCK (DUAL BLOCK)

This type of blockade follows repeated or large doses of depolarizing agents. The tendency is for the depolarizing block to take on the characteristics of a non-depolarizing block. This can be identified with corresponding changes in the pattern of peripheral nerve stimulation. There are five stages described in this process:[48]

1 Typical depolarizing block.
2 Tachyphylaxis: diminished responses to repeated doses.
3 Wedensky inhibition: fade of tetanic stimuli.
4 Fade and potentiation: post-tetanic potentiation present and fade of slow stimuli, e.g., progressive elimination of twitches in train-of-four stimulation.
5 Typical non-depolarizing block which is reversible with anticholinesterase.

The development of this type of block appears to be dependent on cumulative dose of the agent.[49] As well, it may be time-dependent.[50] By defining the change of Phase I to Phase II as a T4 ratio of 0.3 or less, Lee found that the transition was abrupt and usually occurred at a dose of succinylcholine from 3–5 $\text{mg}\cdot\text{kg}^{-1}$.[51] Katz *et al.* also supported a change of Phase I to Phase II block at 3 $\text{mg}\cdot\text{kg}^{-1}$ of succinylcholine, with a gray zone at 2 $\text{mg}\cdot\text{kg}^{-1}$.[52] The mode of administration, infusion or intermittent bolus, did not seem to mater. However, the

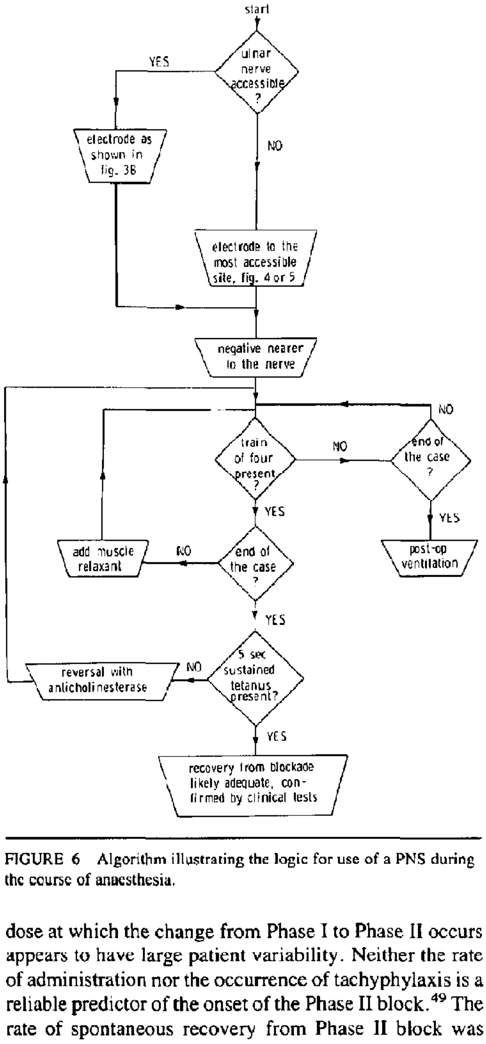

FIGURE 6 Algorithm illustrating the logic for use of a PNS during the course of anaesthesia.

dose at which the change from Phase I to Phase II occurs appears to have large patient variability. Neither the rate of administration nor the occurrence of tachyphylaxis is a reliable predictor of the onset of the Phase II block.[49] The rate of spontaneous recovery from Phase II block was extremely variable, with half of the patients having a prolonged recovery lasting thirty minutes or more.[49] It appears that the time and dose necessary to produce Phase II block depend on the criteria used to define it and the anaesthetic used.[53]

Summary

The use of the peripheral nerve stimulator is essential for adequate assessment of the degree of neuromuscular block. To ensure that the data derived are accurate one must understand the effects of stimulus frequency, electrode type, position and polarity, stimulus intensity, duration, waveform and the various ways used to observe the data, electromechanical, EMG, tactile or visual. Once these features are understood, a better interpretation of the various tests is possible.

TABLE III Minimum requirements of a peripheral nerve stimulator

Single twitch 1 per second
Train of four
Tetanus at 50 Hz
Current output up to 35 mA
Display of adjustable current
Square wave 0.2 millisec

While a lot of information regarding the proper use of the PNS is derived from meticulous scientific experimentation, it is possible to apply this information for clinical use. Most information is available based on ulnar nerve stimulation. Information on stimulation of other nerves (e.g., current to achieve SMS on the peroneal nerve) is lacking. With this in mind, the authors present in Table III the minimum requirements for a PNS and an algorithm to illustrate use of the PNS, in Figure 6.

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