Neuromuscular Monitoring

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KEY POINTS

• Good evidence-based practice dictates that clinicians always quantitate the extent of neuromuscular block by objective monitoring.

• The neuromuscular block should be adjusted to ensure optimal surgical conditions. In most procedures, one or two responses to train-of-four (TOF) stimulation will suffice.

• Adequate recovery of postoperative neuromuscular function cannot be guaranteed without objective neuromuscular monitoring.

• Objective neuromuscular monitoring is essential for management of neuromuscular blockade intraoperatively and its reversal for postoperative care. Muscle relaxants should not be given in the intensive care unit (see Chapters 34, 35, and 101) without proper monitoring.

• It is impossible to exclude with certainty clinically significant residual neuromuscular block by clinical evaluation of recovery of neuromuscular function.

• Residual postoperative neuromuscular block causes decreased chemoreceptor sensitivity to hypoxia, functional impairment of the pharyngeal and upper esophageal muscles, impaired ability to maintain an open upper airway, and an increased risk of hypoxic events, as well as the development of postoperative pulmonary complications.

• Absence of tactile fade in the response to TOF stimulation, tetanic stimulation, and double-burst stimulation does not exclude significant residual block.

• To exclude clinically significant residual neuromuscular block, the TOF ratio must exceed 0.9 when measured mechanically or electromyographically and 1.0 when measured acceleromyographically.

• Antagonism of the neuromuscular block with a cholinesterase inhibitor should not be initiated before at least two to four responses to TOF stimulation are observed.

• Antagonism of the neuromuscular block achieved by rocuronium and vecuronium can be initiated at all levels of block with the selective relaxant binding agent, sugammadex.

• If sufficient recovery (TOF ≥ 0.9-1.0) has not been documented objectively at the end of the surgical procedure, the neuromuscular block should be antagonized with neostigmine or sugammadex. Minority opinion is that even with a TOF greater than 0.9, neostigmine or sugammadex should still be given.

Clinically significant residual neuromuscular block (i.e., paralysis) cannot be excluded using clinical criteria only and can persist postoperatively. Objective monitoring of the degree of neuromuscular block during and after anesthesia reduces the incidence of residual neuromuscular block and should be part of standard monitoring equipment.

In awake patients, muscle power can be evaluated by tests of voluntary muscle strength, but this is impossible during anesthesia and recovery from anesthesia. Instead, the clinician must use clinical tests to assess muscle power directly and to estimate neuromuscular function indirectly (muscle tone; feel of the anesthesia bag as an indirect measure of pulmonary compliance, tidal volume, and inspiratory force). All these tests, however, are influenced by factors other than the degree of neuromuscular block; therefore, whenever more precise information regarding the status of neuromuscular functioning is desired, the response of muscle to nerve stimulation should be assessed. This procedure also takes into account the considerable variation in individual response and sensitivity to muscle relaxants.

This chapter reviews the basic principles of neuromuscular monitoring and the requirements for effective use of nerve stimulators for peripheral nerve stimulation. It also describes the response to nerve stimulation...
during depolarizing (phase I and phase II) and nondepolarizing neuromuscular block. Finally, methods of evaluating evoked neuromuscular responses with and without the availability of recording equipment are discussed.

**TYPES OF PERIPHERAL NERVE STIMULATION**

Neuromuscular function is monitored by evaluating the muscular response to supramaximal stimulation of a peripheral motor nerve. Two types of stimulation can be used: electrical and magnetic. Electrical nerve stimulation is by far the most commonly used method in clinical practice, and it is described in detail in this chapter. In theory, magnetic nerve stimulation has several advantages over electrical nerve stimulation. It is less painful and does not require physical contact with the body; however, the equipment required is bulky and heavy, it cannot be used for train-of-four (TOF) stimulation, and it is difficult to achieve supramaximal stimulation with this method. As a result, magnetic nerve stimulation is seldom used in clinical anesthesia.

**PRINCIPLES OF PERIPHERAL NERVE STIMULATION**

Whatever method is used for neuromuscular monitoring, the clinician must be familiar with the two terms, supramaximal stimulation and calibration.

**SUPRAMAXIMAL STIMULATION**

The reaction of a single muscle fiber to a stimulus follows an all-or-none pattern. In contrast, the response (the force of contraction) of the whole muscle depends on the number of muscle fibers activated. If a nerve is stimulated with sufficient intensity, all fibers supplied by the nerve will react, and the maximum response will be triggered. After administration of a neuromuscular blocking drug, the response of the muscle decreases in parallel with the number of fibers blocked. The reduction in response during constant stimulation reflects the degree of neuromuscular block.

For the preceding principles to be in effect, the stimulus must be truly maximal throughout the period of monitoring; therefore, the electrical stimulus applied is usually at least 15% to 20% greater than that necessary for a maximal response. For this reason, the stimulus is said to be supramaximal; however, supramaximal electrical stimulation can be painful, which is not a concern during anesthesia, but during recovery the patient may be awake enough to experience the discomfort of nerve stimulation. Therefore, some researchers advocate stimulation with submaximal current during recovery. Although several investigations indicate that testing of neuromuscular function can be reliably performed postoperatively with submaximal stimulation, the accuracy of such monitoring is unacceptable with low current.

**CALIBRATION**

A device used for objective monitoring of the neuromuscular function should be calibrated before the neuromuscular blocking drug is administered. Calibration adjusts the gain of the device to ensure that the observed response to supramaximal stimulation is within the measurement window of the device and as close as possible to the “100% control response.” The calibration procedure varies with the type of device used, but most often it is done with 1.0 Hz single-twitch stimulation. It is especially important to calibrate when the onset and recovery of the neuromuscular block are established with single-twitch stimulation.

In the TOF mode of nerve stimulation, calibration is considered less important because all four responses are amplified equally. Consequently, the TOF ratio is rarely influenced by calibration; however, in patients with very weak or strong responses to nerve stimulation, one or more responses to TOF stimulation might be out of the recording window, and the displayed TOF response might be incorrect. In some devices, supramaximal stimulation is established concurrently with the calibration procedure.

**PATTERNS OF NERVE STIMULATION**

For evaluation of neuromuscular function, the most commonly used patterns of electrical nerve stimulation are single-twitch, TOF, and tetanic. Other patterns, such as posttetanic count (PTC) and double-burst stimulation (DBS) can be valuable in certain clinical situations that are described later.

**SINGLE-TWITCH STIMULATION**

In the single-twitch mode of stimulation, single supramaximal electrical stimuli are applied to a peripheral motor nerve at frequencies ranging from 1.0 Hz (once every second) to 0.1 Hz (once every 10 seconds; Fig. 53-1). The response to single-twitch stimulation depends on the frequency at which the individual stimuli are applied. If the rate of delivery is increased to greater than 0.15 Hz, the evoked response will gradually decrease and stabilize at a lower level. As a result, a frequency of 0.1 Hz is generally used. Because 1-Hz stimulation shortens the time necessary to determine supramaximal stimulation, this frequency is sometimes used during induction of anesthesia; however, the apparent time of onset and length of neuromuscular block depend on the pattern and duration of stimulation. Therefore, results obtained with 1-Hz single-twitch stimulation cannot be compared with results obtained using, for example, 0.1-Hz single-twitch stimulation or TOF stimulation.

**TRAIN-OF-FOUR STIMULATION**

Train-of-four nerve stimulation pattern, as introduced by Ali and associates during the early 1970s, consists of four supramaximal stimuli given every 0.5 seconds (2 Hz; Fig. 53-2). When used continuously, each set (train) of
four stimuli is typically repeated every tenth to twentieth second. Each stimulus in the train causes the muscle to contract, and the “fade” in the train of responses provides the basis for evaluation; that is, dividing the amplitude of the fourth response by the amplitude of the first response provides the TOF ratio. In the control response (the response obtained before the administration of a muscle relaxant), all four responses are ideally the same; the TOF ratio is 1.0. During a partial nondepolarizing block, the ratio decreases (fades) and is inversely proportional to the degree of block. During a partial depolarizing block, no fade occurs in the TOF response; ideally, the TOF ratio is approximately 1.0. Fade in the TOF response after injection of succinylcholine signifies the development of a phase II block (discussed later in the section on depolarizing neuromuscular block).

The advantages of TOF stimulation are most apparent during a nondepolarizing neuromuscular block because the degree of block can be read directly from the TOF response even though a preoperative value is lacking. In addition, TOF stimulation has some advantages over double-burst stimulation and tetanic stimulation; it is less painful and, unlike tetanic stimulation, does not generally influence subsequent monitoring of the degree of neuromuscular block.

**TETANIC STIMULATION**

Tetanic stimulation consists of high-frequency delivery of electrical stimuli (e.g., 30, 50, or 100 Hz). The most commonly used pattern in clinical practice is 50-Hz stimulation given for 5 seconds, although some investigators have advocated the use of 50-, 100-, and even 200-Hz stimulation for 1 second. In normal neuromuscular transmission or during a depolarizing block, the muscle response to 50-Hz tetanic stimulation for 5 seconds is sustained. On the other hand, during a nondepolarizing block and a phase II block after the injection of succinylcholine, the response is not sustained (i.e., fade occurs; Fig. 53-3).

Fade in response to tetanic stimulation is normally considered a presynaptic event (see Chapter 18); the traditional explanation is that at the start of tetanic
When the “margin of safety”\(^{18}\) at the postsynaptic membrane is greater than the amount necessary to evoke a response, the muscle response to tetanic nerve stimulation for 5 seconds (TE), and 1.0-Hz posttetanic twitch stimulation (PTS) during four different levels of nondepolarizing neuromuscular block. During intense block of peripheral muscles (A), no response to any of the forms of stimulation occurs. During less pronounced block (deep block, B and C), there is still no response to TOF stimulation, but posttetanic facilitation of transmission is present. During surgical block (D), the first response to TOF appears and posttetanic facilitation increases further. The posttetanic count (see text) is 1 during very deep block (\(\text{A}\)), 3 during surgical (or moderate) block (\(\text{B}\)), 3 during less deep block (\(\text{C}\)), and 8 during surgical (or moderate) block (\(\text{D}\)).

During intense block of peripheral muscles (A), no response to either tetanic or posttetanic stimulation is visible or by tactile evaluation, even experienced observers are unable to judge the response of tetanic stimulation. In contrast, posttetanic twitch potentiation, which sometimes occurs in mechanical recordings before any neuromuscular blocking drug has been given, is a muscular phenomenon that is not accompanied by an increase in the compound muscle action potential.

Tetanic stimulation is extremely painful, which limits its use in unanesthetized patients. Furthermore, especially in the late phase of neuromuscular recovery, tetanic stimulation can produce lasting antagonism of neuromuscular block in the stimulated muscle such that the response of the tested site may no longer be representative of other muscle groups. Traditionally, tetanic stimulation is used to evaluate residual neuromuscular block. Except in connection with the technique of PTC, tetanic stimulation has little use in everyday clinical anesthesia. If the response to nerve stimulation is recorded, all the information required can be obtained from the response to TOF nerve stimulation. In contrast, if the response to nerve stimulation is evaluated only visually or by tactile evaluation, even experienced observers are unable to judge the response of tetanic stimulation with sufficient certainty to exclude residual neuromuscular block.

**POSTTETANIC COUNT STIMULATION**

Injection of a nondepolarizing neuromuscular blocking drug in a dose sufficient to ensure smooth tracheal intubation causes intense neuromuscular block of peripheral muscles. Because there is no response to TOF and single-twitch stimulation under these conditions, these modes of stimulation cannot be used to determine the degree of block. However, an intense neuromuscular block of the peripheral muscles can be monitored by applying tetanic stimulation (50 Hz for 5 seconds) and observing the posttetanic response to single-twitch stimulation given at 1 Hz starting 3 seconds after the end of tetanic stimulation.\(^{23}\) During intense block, there is no response to either tetanic or posttetanic stimulation (Fig. 53-4). As the period of very intense stimulation, large amounts of acetylcholine are released from immediately available stores in the nerve terminal. As these stores become depleted, the rate of acetylcholine release decreases until equilibrium between mobilization and synthesis of acetylcholine is achieved. Despite this equilibrium, the muscle response to tetanic nerve stimulation is maintained (given normal neuromuscular transmission) because the acetylcholine released is many times greater than the amount necessary to evoke a response. When the “margin of safety”\(^{18}\) at the postsynaptic membrane (i.e., the number of free cholinergic receptors) is reduced by nondepolarizing neuromuscular blocking drugs, a typical reduction in twitch height is seen with a fade during, for example, repetitive stimulation. In addition to this postsynaptic block, nondepolarizing neuromuscular blocking drugs can also block presynaptic neuronal subtype acetylcholine receptors, thereby leading to impaired mobilization of acetylcholine within the nerve terminal (see Chapter 18).\(^{19}\) This effect substantially contributes to fade in the response to tetanic (and TOF) stimulation. Although the degree of fade depends primarily on the degree of neuromuscular block, fade also depends on the frequency (Hz), the length (seconds) of stimulation, and on how often tetanic stimuli are applied. Unless these variables are kept constant, results from different studies using tetanic stimulation cannot be compared.

During partial nondepolarizing block, tetanic nerve stimulation is followed by a posttetanic, slight increase in twitch tension called *posttetanic facilitation* (see Fig. 53-3). This event occurs because the increase in mobilization and synthesis of acetylcholine caused by tetanic stimulation continues for some time after discontinuation of stimulation. The degree and duration of posttetanic facilitation depend on the degree of neuromuscular block, with posttetanic facilitation usually disappearing within 60 seconds of tetanic stimulation. Posttetanic facilitation is evident in electromyographic, kinemyographic, acceleromyographic, and mechanomyographic recordings during partial nondepolarizing neuromuscular block. In contrast, posttetanic twitch potentiation, which sometimes occurs in mechanical recordings before any neuromuscular blocking drug has been given, is a muscular phenomenon that is not accompanied by an increase in the compound muscle action potential.
neuromuscular block dissipates, the first response to posttetric twitch stimulation occurs and is followed by a gradual return of posttetanic twitches until the first response to TOF stimulation reappears. For a given neuromuscular blocking drug, the time until return of the first response to TOF stimulation is related to the number of posttetanic twitch responses present at a given time (i.e., the PTC; Fig. 53-5).

The PTC method is mainly used to assess the degree of neuromuscular block when there is no reaction to single-twitch or TOF nerve stimulation. However, PTC can also be used whenever sudden movements must be eliminated (e.g., during surgery in the airways or ophthalmic surgery). A specific clinical example of the value of PTC occurs in ophthalmic surgery (see Chapter 84). The necessary level of block at the adductor pollicis muscle to ensure paralysis of the diaphragm depends on the type of anesthesia. To ensure elimination of any bucking or coughing in response to tracheobronchial stimulation, a neuromuscular block must be intense (i.e., no response to TOF or PTC stimulation) (Fig. 53-6).

When using the new selective relaxant binding drug, sugammadex for reversing a rocuronium-induced or vecuronium-induced deep or intense block (discussed later), the necessary dose of sugammadex depends on the level of block (see Chapter 35). In this situation, PTC can be used to quantitate the degree of block.

The response to PTC stimulation depends primarily on the degree of neuromuscular block. It also depends on the frequency and duration of tetanic stimulation, the length of time between the end of tetanic stimulation and the first posttetanic stimulus, the frequency of the single-twitch stimulation, and probably the duration of single-twitch stimulation before tetanic stimulation. When the PTC method is used, these variables should be kept constant. In addition, because of interference between PTC stimulation and the actual neuromuscular block within the monitored hand, tetanic stimulation should ideally not be performed more often than every 6 minutes.

### DOUBLE-BURST STIMULATION

DBS consists of two short bursts of 50-Hz tetanic stimulation separated by 750 msec, with a 0.2-msec duration of each square wave impulse in the burst (Fig. 53-7). Although the number of impulses in each burst can vary, DBS with three impulses in each of the two tetanic bursts (DBS3,3) is most commonly used.

In nonparalyzed muscle, the response to DBS3,3 is two short muscle contractions of equal strength. In a partially paralyzed muscle, the second response is weaker than the first, and corresponds to the typical TOF fade (see Fig. 53-7). When measured mechanically, the TOF ratio correlates closely with the DBS3,3 ratio. DBS was developed with the specific aim of improving manual (tactile) detection of residual block under clinical conditions, or during recovery and immediately after surgery; tactile evaluation of the response to DBS3,3 is superior to tactile evaluation of the response to TOF stimulation. However, as shown in Figure 53-8, absence of fade in the manually evaluated response to DBS3,3 (and TOF) does not ensure elimination of any bucking or coughing in response to tracheobronchial stimulation.
During cooling, skin resistance can increase to approximately 5 kΩ, which can cause the current delivered to the underlying nerve to decrease below the supramaximal level and lead to a decrease in the response to stimulation and possible misjudgment in the degree of block used.34 The skin should always be cleansed properly and preferably rubbed with an abrasive before application of the electrodes.34 The skin should be small, approximately 7 to 11 mm in diameter (Fig. 53-9). Otherwise, the current produced in the nonparalyzed muscle.

THE NERVE STIMULATOR

Although many nerve stimulators are commercially available, not all meet the basic requirements for clinical use. The stimulus should produce a monophasic and rectangular waveform, and the length of the pulse should not exceed 0.2 to 0.3 msec. A pulse exceeding 0.5 msec may stimulate the muscle directly or cause repetitive firing. Stimulation at a constant current is preferable to stimulation at a constant voltage because current is the determinant of nerve stimulation. Furthermore, for safety reasons, the nerve stimulator should be battery operated, include a battery check, and be able to generate 60 to 70 mA, but not more than 80 mA. Many commercially available stimulators can deliver just 25 to 50 mA and provide a constant current only when skin resistance ranges from 0 to 2.5 kΩ. These limitations are a disadvantage; during cooling, skin resistance can increase to approximately 5 kΩ, which can cause the current delivered to the nerve to decrease below the supramaximal level and lead to a decrease in the response to stimulation and possible misjudgment in the degree of block used. Ideally, the nerve stimulator should have a built-in warning system or a current level display that alerts the user when the selected current is not delivered to the nerve. The polarity of the electrodes should be indicated, and the apparatus should be capable of delivering the following modes of stimulation: TOF (as both a single train and in a repetitive mode, with TOF stimulation being given every 10 to 20 seconds), single-twitch stimulation at 0.1 and 1.0 Hz, and tetanic stimulation at 50 Hz. In addition, the stimulator should have a built-in time constant system to facilitate PTC. The tetanic stimulus should last 5 seconds and be followed 3 seconds later by the first posttetanic stimulus. If the nerve stimulator does not allow objective measurement of the response to TOF stimulation, at least one DBS mode should be available, preferably DBS3,3. Single-twitch, 1-Hz stimulation is particularly useful in assessing the level of supramaximal stimulation. Tetanus at 100 or 200 Hz is rarely indicated because 50-Hz tetanic stimulation is similar to maximal voluntary muscle contraction. Furthermore, in contrast to 100- and 200-Hz stimulation, 50-Hz tetanic stimulation does not cause fatigue (fade) in nonparalyzed muscle.

STIMULATING ELECTRODES

Electrical impulses are transmitted from stimulator to nerve by means of surface or needle electrodes, the former being the more commonly used in clinical anesthesia. Normally, disposable pregelled silver or silver chloride surface electrodes are used. The actual conducting area should be small, approximately 7 to 11 mm in diameter (Fig. 53-9). Otherwise, the current produced in the underlying nerve may not be adequate.34 The skin should always be cleansed properly and preferably rubbed with an abrasive before application of the electrodes. When a supramaximal response cannot be obtained with surface electrodes, needle electrodes can be used in a few exceptional cases. Although specially coated needle electrodes are commercially available, ordinary steel injection needles often suffice. A sterile technique should be used, and the needles should be placed subcutaneously to avoid direct injury to the underlying nerve.
SITES OF NERVE STIMULATION AND DIFFERENT MUSCLE RESPONSES

In principle, any superficially located peripheral motor nerve can be stimulated. In clinical anesthesia, the ulnar nerve is the most popular site; the median, posterior tibial, common peroneal, and facial nerves are also sometimes used. For stimulation of the ulnar nerve, the electrodes are best applied to the volar side of the wrist (see Fig. 53-9). The distal electrode should be placed approximately 1 cm proximal to the point at which the proximal flexion crease of the wrist crosses the radial side of the tendon to the flexor carpi ulnaris muscle. The proximal electrode should preferably be placed so that the distance between the centers of the two electrodes is 3 to 6 cm (see Fig. 53-9). With this placement of the electrodes, electrical stimulation normally elicits only finger flexion and thumb adduction. If one electrode is placed over the ulnar groove at the elbow, thumb adduction is often pronounced because of stimulation of the flexor carpi ulnaris muscle. When this latter placement of electrodes (sometimes preferred in small children) is used, the active negative electrode should be at the wrist to ensure maximal response. Polarity of the electrodes is less crucial when both electrodes are close to each other at the volar side of the wrist; however, placement of the negative electrode distally normally elicits the greatest neuromuscular response. When the temporal branch of the facial nerve is stimulated, the negative electrode should be placed over the nerve, and the positive electrode should be placed somewhere else over the forehead.

Because different muscle groups have different sensitivities to neuromuscular blocking drugs, results obtained for one muscle cannot be automatically extrapolated to other muscles. The diaphragm is among the most resistant of all muscles to both depolarizing and nondepolarizing neuromuscular blocking drugs. In general, the diaphragm requires 1.4- to 2.0-fold as much muscle relaxant as the adductor pollicis muscle for an identical degree of block (Fig. 53-10). Also of clinical significance is that onset time is normally shorter for the diaphragm than for the adductor pollicis muscle, and the diaphragm recovers from paralysis more quickly than the peripheral muscles (Fig. 53-11). The other respiratory muscles are less resistant than the diaphragm, as are the larynx and the corrugator supercilii muscles. Most sensitive are the abdominal muscles, the orbicularis oculi muscle, the peripheral muscles of the limbs, and the geniohyoid, masseter, and upper airway muscles. From a clinical point of view, the response of the corrugator supercilii to facial nerve stimulation reflects the extent of neuromuscular block of the laryngeal adductor muscles and abdominal muscles better than the response of the adductor pollicis to ulnar nerve stimulation. Furthermore, the upper airway muscles seem to be more sensitive than the peripheral muscles. Although some investigations using acceleromyography have indicated small differences in the response to TOF nerve stimulation in the hand (adductor pollicis muscle) compared to the leg (flexor hallucis brevis muscle), these differences are probably of little clinical significance. When comparing different sites of stimulation, there might be large differences between contralateral limbs (e.g., arm-to-arm variation of ± 20%).

Although the precise source of these differences is unknown, possible explanations may be variations in acetylcholine receptor density, acetylcholine release, acetylcholinesterase activity, fiber composition, innervation ratio (number of neuromuscular junctions), blood flow, and muscle temperature.
of the thumb (the adductor pollicis muscle) acts on a force-displacement transducer (Fig. 53-12). The force of contraction of the thumb (the adductor pollicis muscle) acts on a force-displacement transducer (TD-100; Biometer, Odense, Denmark) placed at the proximal phalanx of the thumb.

Figure 53-11. Evolution of twitch height (mean ± SD) of the diaphragm (blue circles) and the adductor pollicis muscle (yellow circles) in 10 anesthetized patients after the administration of atracurium (0.6 mg/kg). (From Pansard J-L, Chauvin M, Lebrault C, et al: Effect of an intubating dose of succinylcholine and atracurium on the diaphragm and the adductor pollicis muscle in humans, Anesthesiology 67:326, 1987.)

MECHANOMYOGRAPHY

For correct and reproducible measurement of evoked tension, the muscle contraction needs to be isometric. In clinical anesthesia, this condition is most easily achieved by measuring the force of contraction of the thumb after the application of a resting tension of 200 to 300 g (a preload) to the thumb. When the ulnar nerve is stimulated, the thumb (the adductor pollicis muscle) acts on a force-displacement transducer (Fig. 53-12). The force of contraction is then converted into an electrical signal, which is amplified, displayed, and recorded. The arm and hand should be rigidly fixed, and care should be taken to prevent overloading of the transducer. In addition, the transducer should be placed in correct relation to the thumb (i.e., the thumb should always apply tension along the length of the transducer). It is important to remember that the response to nerve stimulation depends on the frequency with which the individual stimuli are applied and that the time used to achieve a stable control response may influence subsequent determination of the onset time and duration of block. Generally, the reaction to supramaximal stimulation increases during the first 8 to 12 minutes after commencement of the stimulation (staircase phenomenon). Therefore, in clinical studies, recording of the control response (before injection of muscle relaxant) should not be made until the response has stabilized for 8 to 12 minutes or a 2- or 5-second 50-Hz tetanic stimulation has been given. Even then, twitch response often recovers to 110% to 150% of the control response after paralysis with succinylcholine. This increase in response, possibly caused by a change in the contractile response of the muscle, normally disappears within 15 to 25 minutes.

Although there are numerous methods for mechanical recording of evoked mechanical responses, not all meet the criteria outlined. Mechanomyography is recognized as the gold standard of neuromuscular monitoring. Despite this status, there is no commercially available neuromuscular monitor for daily clinical use based on this principle.

Figure 53-12. The setup for mechanomyography. The response to nerve stimulation is measured using a force transducer (TD-100; Biometer, Odense, Denmark) placed at the proximal phalanx of the thumb.

RECORDING OF EVOKED RESPONSES

Five methods are available for clinical monitoring of neuromuscular function: evoked mechanical response of the muscle (mechanomyography [MMG]), evoked electrical response of the muscle (electromyography [EMG]), acceleration of the muscle response (acceleromyography [AMG]), evoked electrical response in a piezoelectric film sensor attached to the muscle (kinemyography [KMG]) and measurement of low-frequency sounds evoked by the muscle contraction (phonomyography [PMG]). The five methods are described below. For further information on recording evoked responses, the reader is referred to guidelines for good clinical research practice in pharmacodynamic studies of neuromuscular blocking drugs. The only objective monitors currently available are based on AMG, EMG, and KMG. The use of computer-guided administration of neuromuscular blocking drugs and “closed loop control” systems has been suggested, but no systems are commercially available.

ELECTROMYOGRAPHY

Evoked EMG records the compound action potentials produced by stimulation of a peripheral nerve. The compound action potential is a high-speed event that for many years could be detected only by means of a preamplifier and a storage oscilloscope. Modern neuromuscular transmission analyzers are able to make online electronic analyses and graphic presentations of the EMG response. The evoked EMG response is most often obtained from muscles innervated by the ulnar or the median nerves. Stimulating electrodes are applied as in force measurements. Although both surface and needle electrodes can be used for recording, no advantage is obtained by using the latter. Most often, the evoked EMG response is obtained from the thenar or hypothenar eminence of the hand or from the first dorsal intersosseous muscle of the hand, preferably with the active electrode over the motor
As is the case with surface laryngeal EMG, surface diaphragmatic EMG may differ. Although evoked EMG records changes associated with excitation-contraction coupling and contraction of the phrenic muscle, the results obtained with these methods may differ. For these reasons, the results obtained with evoked EMG are highly sensitive to electrical interference, inadequate fixation of the hand, or changes in temperature that the EMG response often does not return to the control level. Whether this situation is the result of technical problems, inadequate fixation of the hand, or changes in temperature is unknown (Fig. 53-14). Finally, the evoked EMG response is highly sensitive to electrical interference, such as that caused by diathermy.

ACCELEROMYOGRAPHY

The technique of AMG is based on Newton’s second law: Force = Mass × Acceleration. If mass is constant, acceleration is directly proportional to force. Accordingly, after nerve stimulation, one can measure not only the evoked force but also acceleration of the thumb.

AMG uses a piezoelectric ceramic wafer with electrodes on both sides. Exposure of the electrode to a force generates an electrical voltage proportional to acceleration of the electrode. Consequently, when an accelerometer is fixed to the thumb and the ulnar nerve is stimulated, an electrical signal is produced whenever the thumb moves. This signal can be analyzed in a specially designed analyzer or displayed on a recording system. At least two detached monitors are commercially available, based on the same transducer: the TOF-Watch (Biometer, Odense, Denmark) and the Infinity Trident NMT SmartPod (Dräger, Lübeck, Germany; Fig. 53-15).
AMG is a simple method of analyzing neuromuscular function, both in the operating room and in the intensive care unit. Although good correlation exists between the TOF ratio measured by this method and the TOF ratio measured with a force-displacement transducer or EMG, measurements made via AMG are not directly comparable with results obtained by the other two methods. When AMG is used with a free-moving thumb, as originally suggested, wide limits of agreements in twitch height (T1) and TOF ratio and differences in the onset and recovery course of block between AMG and MMG have been found. Moreover, the AMG control TOF ratio is consistently higher when measured with a force-displacement transducer. In accordance with this, several studies have indicated that when using AMG, the TOF ratio indicative of sufficient postoperative neuromuscular recovery is 1.0 rather than 0.9, as when measured by MMG or EMG in the adductor pollicis muscle. In contrast to MMG and EMG, the control baseline TOF value before administration of a neuromuscular blocking drug is most often 1.1 to 1.2 when measured with AMG, and in some patients is as high as 1.4. A high control baseline value probably indicates that the TOF ratio necessary for excluding residual curarization is equally higher. For instance, in a patient with a high control baseline value (e.g., TOF = 1.2), it is to be expected that a higher TOF ratio during recovery is necessary to exclude residual block compared with a patient with a low control baseline value (e.g., TOF = 0.95). It is generally accepted that the TOF ratio should be at least 0.90 to exclude clinically significant residual paralysis; using the preceding example, a TOF ratio of 1.08 (90% of 1.2) would represent safe recovery in the first patient, whereas a TOF ratio of 0.86 (90% of 0.95) would suffice in the other patient. To overcome such problems, it has been suggested to refer to the actually obtained TOF ratios during recovery to the baseline control TOF ratio (normalization). Currently, no commercially available monitors can “normalize” the TOF ratio automatically. Intuitively, for excluding residual block using AMG, a TOF ratio of at least 1.0 should be targeted to exclude residual block.

One reason for the wide limits of agreement between AMG and MMG is probably and paradoxically connected with one of the originally claimed advantages of the method, that fixation of the hand could be reduced to a minimum as long as the thumb could move freely. In clinical practice, it is often not possible to ensure that the thumb can move freely and that the position of the hand does not change during the surgical procedure. The evoked response can therefore vary considerably. Several solutions have been proposed, but the use of an elastic preload on the thumb improves the precision without compromising the agreement between results obtained with AMG and MMG. Studies have indicated that objective monitoring with AMG reduces and almost eliminates the problem of postoperative residual neuromuscular block.

When the thumb is not available for monitoring during surgery, some clinicians prefer to monitor the AMG response of the orbicularis oculi or the corrugator supercilii in response to facial nerve stimulation. The technique of the piezoelectric monitor is based on the principle that stretching or bending a flexible piezoelectric film (e.g., one attached to the thumb) in response to nerve stimulation generates a voltage that is proportional to the amount of stretching or bending. At least one device based on this principle is available commercially in two sizes (adult and pediatric): the NMT MechanoSensor (Datex-Ohmeda, Helsinki, Finland; Fig. 53-17).

Few studies have evaluated the function of these monitors. Limited data indicate not only a good relationship between results obtained with PZEMG, AMG, and MMG, but also wide limits of agreement between

**Piezoelectric Neuromuscular Monitors**

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Few studies have evaluated the function of these monitors. Limited data indicate not only a good relationship between results obtained with PZEMG, AMG, and MMG, but also wide limits of agreement between
the methods. Therefore, although PZEMG may be a valuable clinical tool, the values obtained in an individual patient with this method can vary from those obtained with MMG or AMG.

PHONOMYOGRAPHY

Phonomography (acoustic myography) is an interesting new method of monitoring neuromuscular function, but it is not yet commercially available.\(^4^9,8^6-9^1\) Contraction of skeletal muscles generates intrinsic low-frequency sounds, which can be recorded with special microphones. This method has been evaluated for clinical and research purposes. Several reports indicate good correlation between evoked acoustic responses and those obtained with more traditional methods of recording, such as MMG, EMG, and AMG. However, it is uncertain whether PMG will ever be used for monitoring neuromuscular block during routine anesthesia. What does make PMG interesting, however, is that in theory the method can be applied not only to the adductor pollicis muscle, but also to other muscles of interest such as the diaphragm, larynx, and eye muscles. In addition, the ease of application is attractive.

EVALUATION OF RECORDED EVOKED RESPONSES

Nerve stimulation in clinical anesthesia is usually synonymous with TOF nerve stimulation. Therefore, the recorded response to this form of stimulation is used to explain how to evaluate the degree of neuromuscular block during clinical anesthesia.

NONDEPOLARIZING NEUROMUSCULAR BLOCK

After injection of a nondepolarizing neuromuscular blocking drug in a dose sufficient for smooth tracheal intubation, TOF recording demonstrates four phases, or levels, of neuromuscular block: intense block, deep block, moderate or surgical block, and recovery (Fig. 53-18).

**Intense Neuromuscular Block**

Intense or profound neuromuscular block occurs within 3 to 6 minutes of injection of an intubating dose of a nondepolarizing muscle relaxant, depending on the drug and the dose given. This phase is also called the “period of no response” because no response to any pattern of nerve stimulation occurs. The length of this period varies, again depending primarily on the duration of action of the muscle relaxant and the dose given. The sensitivity of the patient to the drug also affects the period of no response. An intense block cannot be antagonized with a cholinesterase inhibitor (e.g., neostigmine), and only a high dose of sugammadex (16 mg/kg) can antagonize an intense block caused by rocuronium or vecuronium.\(^9^2,9^3\)

**Deep Neuromuscular Block**

Intense neuromuscular block is followed by a period of deep neuromuscular block, characterized by absence of...
response to TOF stimulation, but with the presence of posttetanic twitches (i.e., PTC ≥ 1; compare with Figure 53-4). Although prediction of the duration of a deep neuromuscular block is difficult, correlation usually exists between PTC stimulation and the time until reappearance of the first response to TOF stimulation (see Fig. 53-5). Attempts to reverse a deep neuromuscular block with neostigmine or vecuronium can be antagonized completely within a few minutes using a dose of sugammadex of 4 mg/kg.13-16

**Moderate or Surgical Neuromuscular Block**

Moderate or surgical neuromuscular block begins when the first response to TOF stimulation appears. This phase is characterized by a gradual return of the four responses to TOF stimulation. Furthermore, good correlation exists between the degree of neuromuscular block and the number of responses to TOF stimulation. When only one response is detectable, the degree of neuromuscular block (the depression in twitch tension) is 90% to 95%. When the fourth response reappears, neuromuscular block is usually 60% to 85%.17 The presence of one or two responses in the TOF pattern normally indicates sufficient relaxation for most surgical procedures. During light anesthesia, however, patients may move, buck, or cough; therefore, a deeper block (or a deeper level of anesthesia) may be necessary when elimination of sudden movements or facilitation of surgery is necessary. The deep neuromuscular block can then be evaluated with PTC (see Fig. 53-6).23

Antagonism of neuromuscular block with neostigmine should usually not be attempted when the block is intense or deep. Even if some reversal occurs, it will often be inadequate, regardless of the dose of neostigmine administered.18 Furthermore, after the administration of large doses of muscle relaxants, reversal of the block with neostigmine to clinically normal activity is not always possible if only one TOF response is present. In general, antagonism with neostigmine should not be initiated before at least two to four responses are observed. Even then, sufficient recovery cannot be guaranteed unless documented using objective monitoring (see Chapter 35).19,20

Antagonism of moderate block induced by rocuronium and vecuronium can be achieved with a small dose of sugammadex (2 mg/kg) within a few minutes.21-23 However, the reappearance of neuromuscular blockade has been reported by anesthesiologists from Japan24 when the 2 mg/kg dose has been used. They did not monitor the degree of neuromuscular blockade. Did the reappearance of neuromuscular blockade occur because of inadequate monitoring or too small a dose of sugammadex? Even with proper monitoring, these results suggest that a dose larger than 2 mg/kg should be used.24 Although the antagonism of neuromuscular block from sugammadex seems to be fast and predictable, objective monitoring should still be used until the TOF ratio is 0.9 to 1.0.

**Recovery from Neuromuscular Block**

Return of the fourth response in the TOF heralds the recovery phase. During neuromuscular recovery, a reasonably good correlation exists between the actual TOF ratio and clinical observation, but the relationship between the TOF ratio and signs and symptoms of residual block varies greatly among patients.80,81 When the TOF ratio is 0.4 or less, the patient is generally unable to lift the head or arm. Tidal volume may be normal, but vital capacity and inspiratory force is reduced. When the ratio is 0.6, most patients are able to lift their head for 3 seconds, open their eyes widely, and stick out their tongue, but vital capacity and inspiratory force are often still reduced. At a TOF ratio of 0.7 to 0.75, the patient can normally cough sufficiently and lift the head for at least 5 seconds, but grip strength may still be as low as about 60% of control.80 When the ratio is 0.8 and higher, vital capacity and inspiratory force are normal.17,82,83 The patient may, however, still have diplopia, blurred vision, and facial weakness (Table 53-1).80,81

The TOF ratio must exceed 0.90 when recorded with MMG or EMG, and 1.0 when using AMG to exclude clinically important residual neuromuscular block.30,34,67,68,70,111-116 Moderate degrees of neuromuscular block can impair carotid body chemosensitivity to hypoxia with absent ventilatory response to arterial desaturation.111-114,116 Moreover, residual block (TOF < 0.90) is associated with functional impairment of the pharyngeal and upper esophageal muscles, which most probably predisposes to regurgitation and aspiration of gastric contents.44 Eikermann and colleagues have documented that partial neuromuscular block, even to a degree that does not evoke dyspnea or oxygen desaturation, can decrease inspiratory upper airway volume and can evoke partial inspiratory airway collapse.117 Also, residual block (TOF < 0.70) caused by the long-acting muscle relaxant pancuronium is a significant risk factor for the development of postoperative pulmonary complications (Table 53-2 and Fig. 53-19).113 Intraoperative neuromuscular monitoring reduces the risk of residual neuromuscular block and results in fewer patients with hypoxic events or airway obstruction in the postesthesia care unit.79 Even in volunteers without sedation or impaired consciousness, a TOF ratio of 0.90 or less

**TABLE 53-1 CLINICAL SIGNS AND SYMPTOMS OF RESIDUAL PARALYSIS IN AWAKE VOLUNTEERS AFTER MIVACURIUM-INDUCED NEUROMUSCULAR BLOCK**

<table>
<thead>
<tr>
<th>Train-of-Four Ratio</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.70-0.75</td>
<td>Diplopia and visual disturbances</td>
</tr>
<tr>
<td></td>
<td>Decreased handgrip strength</td>
</tr>
<tr>
<td></td>
<td>Inability to maintain apposition of the incisor teeth</td>
</tr>
<tr>
<td>&quot;Tongue depressor test&quot; negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe facial weakness</td>
</tr>
<tr>
<td>0.85-0.90</td>
<td>Overall weakness and tiredness</td>
</tr>
<tr>
<td></td>
<td>Diplopia and visual disturbances</td>
</tr>
<tr>
<td></td>
<td>Generalized fatigue</td>
</tr>
</tbody>
</table>

From 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 86:765, 1997.
can impair the ability to maintain the airway. In summary, adequate recovery of neuromuscular function requires the return of an MMG or EMG TOF ratio to at least 0.90, and an AMG TOF ratio to at least 1.0 (or normalized to 0.90), which cannot be guaranteed without objective neuromuscular monitoring.

### DEPOLARIZING NEUROMUSCULAR BLOCK (PHASE I AND II BLOCKS)

Patients with normal plasma cholinesterase activity who are given a moderate dose of succinylcholine (0.5 to 1.5 mg/kg) undergo a typical depolarizing neuromuscular block (phase I block; i.e., the response to TOF or tetanic stimulation does not fade, and no posttetanic facilitation of transmission occurs). In contrast, some patients with genetically determined abnormal plasma cholinesterase activity who are given the same dose of succinylcholine undergo a nondepolarizing-like block characterized by fade in the response to TOF and tetanic stimulation and the occurrence of posttetanic facilitation of transmission (Fig. 53-20). This type of block is called a phase II block (dual, mixed, or desensitizing block). In addition, phase II blocks sometimes occur in genetically normal patients after repetitive bolus doses or a prolonged infusion of succinylcholine.

From a therapeutic point of view, a phase II block in normal patients must be differentiated from a phase II block in patients with abnormal cholinesterase activity. In healthy patients, a phase II block can be antagonized by administering a cholinesterase inhibitor a few minutes after discontinuation of succinylcholine. In patients with abnormal genotypes, however, the effect of intravenous injection of a cholinesterase inhibitor (e.g., neostigmine) is unpredictable because it inhibits acetylcholinesterase and plasma-cholinesterase. For example, neostigmine can potentiate the block dramatically, temporarily improve neuromuscular transmission, and then potentiate the block or partially reverse the block, all depending on the time elapsed since administration of succinylcholine and the dose of neostigmine given. Therefore, unless the cholinesterase genotype is known to be normal, antagonism of a phase II block with a cholinesterase inhibitor should be undertaken with extreme caution. Even if

#### TABLE 53-2 RELATIONSHIP BETWEEN TRAIN-OF-FOUR RATIO AT THE FIRST POSTOPERATIVE RECORDING AND POSTOPERATIVE PULMONARY COMPLICATIONS

<table>
<thead>
<tr>
<th></th>
<th>Pancuronium (n = 226)</th>
<th>Atracurium or Vecuronium (n = 450)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with POPC</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>TOF ≥ 0.70</td>
<td>167</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 4.8%</td>
</tr>
<tr>
<td></td>
<td>TOF &lt; 0.70</td>
<td>59 16.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 4.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23 5.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 4.2%</td>
</tr>
</tbody>
</table>

*Results from a prospective, randomized, and blinded study of postoperative pulmonary complications (POPC) in a total of 691 adult patients undergoing abdominal, gynecologic, or orthopedic surgery and receiving either pancuronium, atracurium, or vecuronium. In 4 of the 46 patients with POPC (3 in the pancuronium group and 3 in the atracurium and vecuronium groups), the train-of-four (TOF) ratio was not available. Because there were no significant differences in the two groups of patients given the intermediate-acting muscle relaxants, the data from these groups are pooled.

†p < 0.02 versus patients in the same group with a train-of-four ratio of 0.70 or greater.

### Figure 53-19

Predicted probabilities of a postoperative pulmonary complication (POPC) in different age groups in orthopedic, gynecologic, and major abdominal surgery with duration of anesthesia of less than 200 minutes. The red lines represent patients with residual neuromuscular block (train-of-four [TOF] < 0.70) after the administration of pancuronium; the blue lines represent patients with a TOF of 0.70 or greater after the administration of pancuronium, as well as all patients after the administration of atracurium and vecuronium, independent of the TOF ratio at the end of anesthesia.
neuromuscular function improves promptly, patient surveillance should continue for at least 1 hour.

USE OF NERVE STIMULATORS IN DAILY CLINICAL PRACTICE

Whenever a neuromuscular blocking drug is administered to a patient, objective monitoring of the evoked response using recording equipment is the best way to evaluate the neuromuscular block. However, tactile or visual evaluation are still the most common forms of clinical neuromuscular monitoring, not least when recording equipment is not available or considered unreliable. The following is a description of how to use nerve stimulators with or without recording equipment (objective monitoring).

PREPARATIONS BEFORE INDUCTION OF ANESTHESIA AND ADMINISTRATION OF THE NEUROMUSCULAR BLOCKING AGENT

First, for supramaximal stimulation, careful cleansing of the skin and proper placement and fixation of electrodes are essential. When the ulnar nerve is used for nerve stimulation, one should take advantage of the fact that the nerve follows the artery by placing the electrodes above the pulse. This placement gives the best response (see Fig. 53-5). Second, every effort should be taken to prevent central cooling, as well as cooling of the extremity being evaluated. Both central and local surface cooling of the adductor pollicis muscle can reduce twitch tension and the TOF ratio. Peripheral cooling can affect nerve conduction, decrease the rate of release of acetylcholine and muscle contractility, increase skin impedance, and reduce blood flow to the muscles, thus decreasing the rate of removal of muscle relaxant from the neuromuscular junction. These factors might account for the occasional and pronounced difference in muscle response between a cold extremity and the contralateral warm extremity.

USE OF A NERVE STIMULATOR DURING INDUCTION OF ANESTHESIA

The nerve stimulator should be attached to the patient before induction of anesthesia, but should not be turned on until after the patient is unconscious.

Single-twitch stimulation at 1 Hz can be used initially when seeking supramaximal stimulation. However, after supramaximal stimulation has been ensured and before the muscle relaxant is injected, the recording equipment (when using objective monitoring) should be calibrated to ensure that the response is in the measurement window and the response to 1 Hz stimulation is set to 100%. Currently, all commercially available devices have an automatic calibration modus. Without calibration, the recorded response to nerve stimulation might differ significantly from the visual or tactile response throughout all levels of neuromuscular block; therefore, the mode of stimulation should be changed to TOF (or 0.1-Hz twitch stimulation). When the response to this stimulation is observed (the control response), the neuromuscular blocking drug is injected. Although the trachea is often intubated when the response to TOF stimulation disappears, postponement of this procedure for 30 to 90 seconds, depending on the muscle relaxant used, usually produces better conditions.

When possible, the response to nerve stimulation should be evaluated at the thumb (rather than at the fifth finger). Direct stimulation of the muscle often causes subtle movement of the fifth finger when no response is present at the thumb. Finally, the different sensitivities of various muscle groups to neuromuscular blocking drugs should always be kept in mind.

USE OF A NERVE STIMULATOR DURING SURGERY

If tracheal intubation is facilitated by the administration of succinylcholine, no more muscle relaxant should be given until the response to nerve stimulation reappears or the patient shows other signs of returning neuromuscular function. If plasma cholinesterase activity is normal, the muscle response to TOF nerve stimulation reappears within 4 to 8 minutes.

When a nondepolarizing neuromuscular drug is used for tracheal intubation, a longer-lasting period of intense block usually follows. During this period of no response to TOF and single-twitch stimulation, the time until the return of response to TOF stimulation can be evaluated by PTC (see Fig. 53-5 and Fig. 53-21).

For most surgical procedures requiring muscle relaxation, it is not necessary to have an intense block, provided that the patient is adequately anesthetized. If a nondepolarizing relaxant is used, a moderate level of neuromuscular block with one or two of the responses to TOF stimulation is sufficient. However, because the respiratory muscles (including the diaphragm) are less sensitive to neuromuscular blocking drugs than the peripheral

Figure 53-20. Typical recording of the mechanical response to train-of-four ulnar nerve stimulation after injection of 1 mg/kg of succinylcholine (arrow) in a patient with genetically determined abnormal plasma cholinesterase activity. The prolonged duration of action and the pronounced fade in the response indicate a phase II block.
muscles are, the patient may breathe, hiccup, or even cough at this depth of block. Moreover, tonus of the diaphragm might impede the surgical conditions. To ensure paralysis of the diaphragm, neuromuscular block of the peripheral muscles must be so intense that the PTC is zero at the thumb.

The disadvantages of sustaining a deep or intense neuromuscular block is that the risk of awareness most probably is increased (see Chapters 13 and 50). When muscles are completely paralyzed, the patient cannot signal awareness with voluntary or involuntary movements. Another disadvantage of a deep or intense block is that the neuromuscular block cannot readily be reversed by neostigmine. Only sugammadex can reverse a deep or intense neuromuscular block (if caused by rocuronium or vecuronium; see Chapter 35).

**USE OF A NERVE STIMULATOR DURING REVERSAL OF NEUROMUSCULAR BLOCK**

Antagonism of nondepolarizing neuromuscular block is most often facilitated with a cholinesterase inhibitor, such as neostigmine, or with the selective relaxant binding agent sugammadex when the neuromuscular block is achieved using rocuronium or vecuronium.

Antagonism with neostigmine should not be initiated before at least two to four responses to TOF stimulation are present or before there are obvious clinical signs of returning neuromuscular function. Reversal of neuromuscular block will not be hastened and can possibly be delayed by giving neostigmine when no response to peripheral nerve stimulation is present. Moreover, even when there are two to four responses to TOF stimulation, the reversal is slow and insufficient in some patients. With a large dose of neostigmine (e.g., 5 mg/70 kg) the median time to achieve a TOF ratio of 0.90 is 15 to 20 minutes, and it will take approximately 90 to 120 minutes to achieve a TOF ratio of 0.90 in 95% of the patients after an intermediate-acting neuromuscular blocking drug (e.g., rocuronium). Conversely, a large dose of neostigmine after full recovery might give a paradoxical block with decreasing TOF ratio.127-131

When rocuronium or vecuronium is used, the selective relaxant binding drug, sugammadex can be used for reversal102,103 (see Chapter 35). Sugammadex encapsulates rocuronium and vecuronium with a high affinity, thereby antagonizing the neuromuscular blocking effect. Three different doses of sugammadex are recommended according to the level of block. A large dose (16 mg/kg) is given during intense block (no response to PTC stimulation).92,93 a medium dose (4 mg/kg) during deep block (two or more responses to PTC),94-96 and a low dose (2 mg/kg) during moderate block (two or more responses to TOF stimulation).102-104 In most patients, all levels of neuromuscular block are reversed within 2 to 5 minutes. However, residual neuromuscular block can be excluded only with objective monitoring (TOF ratio, 0.9 to 1.0).132

As previously described, a recent observational study from Japan also placed emphasis on the relative relationship between a dose of sugammadex and monitoring of neuromuscular blockade.105 Basically, Kotake and colleagues observed reappearance of neuromuscular block after administration of an average dose of 2.7 mg/kg of sugammadex. The accompanying editorial by Naguib and colleagues placed prime importance on the lack of monitoring as the problem. They also lamented the frequent incidence of not using neuromuscular monitoring during anesthesia. The emphasis on monitoring is important and correct, but incomplete. In this editor’s (R. D. Miller) opinion, a larger dose of sugammadex should be given. However, Naguib and colleagues state that this recommendation would double the cost of the reversal drug. Should we not give a proper dose of sugammadex in the interest of decreasing the incidence of residual neuromuscular block? The fact that these two publications are being referenced twice within this chapter indicates their importance.

During recovery of neuromuscular function, when all four responses to TOF stimulation can be felt, an estimation of the TOF ratio can be attempted. However, manual (tactile) evaluation of the response to TOF stimulation (see Fig. 53-8) is not sensitive enough to exclude the possibility of residual neuromuscular block.22,29,119,133 Greater sensitivity is achieved with DBS3,3, but even absence of manual

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**Figure 53-21.** Diagram showing when the different modes of electrical nerve stimulation can be used during clinical anesthesia. Dark areas indicate appropriate use and light areas, less effective use. Modes of nerve stimulation are train-of-four (TOF) stimulation; posttetanic count (PTC); double-burst stimulation (DBS); and the question mark (?), indicating that TOF is less useful in the recovery room unless measured with mechanical, electromyography, or acceleromyography. (See text for further explanation.)

**Table 53-2.** Table showing the effect of different nerve stimulations on neuromuscular block. Single twitch data: 1.0 Hz, 0.1 Hz, and TOF, PTC, DBS during recovery room.
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fade in the DBS$_{3,3}$ response does not exclude clinically significant residual block. Moreover, some patients might suffer from residual block, even after recovery to a TOF ratio of 0.9 to 1.0. Therefore, manual evaluation of responses to nerve stimulation should always be considered in relation to reliable clinical signs and symptoms of residual neuromuscular block (Box 53-1).

WHEN TO USE A PERIPHERAL NERVE STIMULATOR

In clinical practice, significant residual block can be excluded with certainty only if an objective method of neuromuscular monitoring is used. Therefore, good evidence-based practice dictates that clinicians should always quantitate the extent of neuromuscular recovery by objective monitoring. Only a TOF ratio of 0.90 to 1.00 that is measured by objective monitoring ensures a low risk of clinically significant residual block.

However, in many departments clinicians do not have access to equipment for measuring the degree of block. How then to evaluate and, as far as possible, exclude a clinically significant postoperative block? First, long-acting neuromuscular blocking drugs should not be used. Second, the tactile response to TOF nerve stimulation should be evaluated during surgery. Third, if possible, total twitch suppression should be avoided. The neuromuscular block should be managed so that there are always one or two tactile TOF responses. Fourth, the block should be antagonized at the end of the procedure, preferably with sugammadex if rocuronium or vecuronium have been used. When using neostigmine, reversal should not be initiated before at least two to four responses to TOF stimulation are present. Fifth, during recovery, tactile evaluation of the response to DBS is preferable to tactile evaluation of the response to TOF stimulation because it is easier to manually assess fade in the DBS than in the TOF response. Sixth, the clinician should recognize that the absence of tactile fade in both the TOF and DBS responses does not exclude significant residual block. Finally, reliable clinical signs and symptoms of residual block (see Box 53-1) should be considered in relation to the response to nerve stimulation. Figure 53-22 shows how to minimize the risk of residual block with or without objective monitoring.

In view of the uncertainty connected with the use of clinical tests of postoperative neuromuscular recovery and tactile evaluation of the response to nerve stimulation, all patients receiving neuromuscular blocking drugs should be monitored with an objective monitor (also see Chapter 35). Whether the functioning of such a neuromuscular transmission analyzer is based on EMG, MMG, AMG, PZEMG, or PMG is not crucial, as long as the apparatus is used appropriately.

Complete references available online at expertconsult.com
Reversal when *quantitative* (objective) neuromuscular monitoring is available and reliable

- Reversal with sugammadex (SUG)
  - No response to TOF
    - PTC 0
    - SUG 16 mg/kg
  - TOF count 1–4
    - PTC 1–15
    - SUG 4 mg/kg
  - TOF ratio < 1.0
    - TOF < 0.9
      - SUG 2 mg/kg
    - TOF ≥ 0.9
      - SUG 2 mg/kg
  - No response
    - SUG 2 mg/kg

- Reversal with neostigmine (NEO)
  - TOF ≥ 0.9
    - TOF 0.4–0.9
      - TOF count 2–3
      - NEO 0.05 mg/kg
    - TOF < 0.4 or TOF count 0–1
      - Delay reversal to the TOF count of 2

Reversal when *peripheral* (subjective) nerve stimulator is available only or quantitative neuromuscular monitoring is unreliable

- Reversal with sugammadex (SUG)
  - No response to TOF
    - PTC 0
    - SUG 16 mg/kg
  - TOF count 1–4 with or without fade
    - PTC 1–15
    - SUG 4 mg/kg
  - TOF count 2–4
    - Delays reversal to the TOF count of 2
    - SUG 2 mg/kg

- Reversal with neostigmine (NEO)
  - No response to TOF
    - NEO 0.02 mg/kg
  - TOF count 2–3
    - NEO 0.05 mg/kg
  - TOF count 4
    - NEO 0.04 mg/kg

**Figure 53-22.** Suggestion to diminish the incidence of residual curarization by neostigmine or sugammadex according to the level of block, determined with a nerve stimulator (quantitative or peripheral). Note that only a quantitative measured TOF ratio of 0.90 to 1.00 ensures low risk of clinically significant residual block. PTC, Posttetanic count; TOF, train-of-four. *(Modified from Kopman AF, Eikermann M: Antagonism of non-depolarising neuromuscular block: current practice, Anaesthesia 64[Suppl 1]:22-30, 2009.)*
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