Residual neuromuscular blockade: incidence, assessment, and relevance in the postoperative period

G. S. MURPHY

Department of Anesthesiology
Evanston Northwestern Healthcare
Northwestern University
Feinberg School of Medicine, IL, USA

The residual effects of neuromuscular blocking agents may persist into the early postoperative recovery period, even when neuromuscular blockade is carefully monitored and reversed in the operating room. Recent data suggest that mild degrees of residual paresis (train-of-four TOF ratios of 0.7-0.9) may be associated with significant impairment of respiratory and pharyngeal muscle function. Therefore, the new gold standard reflecting acceptable neuromuscular recovery is a TOF ratio \( \geq 0.9 \). Several investigations have demonstrated that many patients continue to arrive in the postanesthesia care unit with TOF ratios <0.7-0.9. Several techniques may be used to reduce the risk of postoperative residual paresis, which include avoidance of long-acting muscle relaxants, use of neuromuscular monitoring in the operating room, routine reversal of neuromuscular blockade at a TOF count of 2-3, and early administration of reversal agents. Careful management of neuromuscular blockade may limit the occurrence of adverse events associated with residual postoperative paralysis. Large-scale outcome studies are needed to clearly define the impact of residual neuromuscular block on major morbidity and mortality in surgical patients.

Key words: Neuromuscular blockage - Paresis - Paralysis - Neuromuscular blocking agents - Neuromuscular monitoring - Acceleromyography - Train-of-four ratio.

Funding provided by the Department of Anesthesiology, Evanston Northwestern Healthcare.

Address reprint requests to: G. S. Murphy, MD, Department of Anesthesiology, Evanston Northwestern Healthcare, 2650 Ridge Ave., Evanston, Ill. 60201, USA. E-mail: gmurphy@enh.org

Residual neuromuscular blockade is frequently observed in the Post Anesthesia Care Unit (PACU) when neuromuscular blocking agents (NMBAs) are administered in the operating room. The presence of significant muscle weakness is commonly documented in the early postoperative period, even when intermediate-acting NMBAs are used and routinely monitored and reversed.

The impact of residual neuromuscular block on major adverse outcomes following surgery has been poorly studied. However, studies suggest that the residual effects of NMBAs can prolong postoperative recovery, adversely affect respiratory function, impair airway protective reflexes, and produce unpleasant symptoms of muscle weakness. The purpose of this article is to review the definitions of residual neuromuscular blockade, to discuss the incidence and consequences of this complication in the early postoperative period, and to describe methods to reduce the frequency of residual paresis following general anesthesia.
Residual neuromuscular block has been defined by correlating signs and symptoms of muscle weakness with train-of-four (TOF) fade ratios in volunteer studies. In the mid-1970s, data suggested that TOF ratios of 0.7 were associated with clinically acceptable values for vital capacity, inspiratory force, and peak expiratory flow rates. For the next 2 decades, a TOF ratio ≥ 0.7 was considered a gold standard value which represented adequate neuromuscular recovery. Recent studies in awake volunteers have documented that TOF ratios of 0.7-0.9 are associated with impaired airway protective reflexes, upper airway obstruction, a decreased hypoxic ventilatory response, and unpleasant symptoms of muscle weakness. This data clearly demonstrates that neuromuscular recovery is incomplete at a TOF ratio of 0.7, and that the new gold standard for acceptable recovery should be a TOF ratio of ≥ 0.9. Most clinical trials examining postoperative residual paresis now use a TOF ratio < 0.9 to define incomplete neuromuscular recovery.

### Incidence of postoperative residual neuromuscular blockade

In 1979, Viby-Mogensen et al. determined the incidence of postoperative residual paralysis by measuring TOF fade ratios in the PACU. All patients received long-acting NMBA in the operating room. Despite apparent clinical recovery, 42% of patients had TOF ratios < 0.7. Subsequent clinical investigators confirmed that a high percentage (21-39%) of patients administered long-acting NMBA had TOF ratios < 0.7 in the PACU. The frequent occurrence of severe postoperative residual paresis following the use of long-acting NMBA is a well-known complication of these drugs, and has resulted in the gradual elimination of these agents from most clinical practices.

Clinical trials have compared the incidence of postoperative residual paresis following the use of long- and intermediate-acting NMBA (Table I). These studies demonstrate that the risk of observing a TOF ratio < 0.7 in the PACU is reduced when shorter-acting agents are administered. Although the presence of postoperative residual neuromuscular block appears to be related to the duration of action of the NMBA, several recent studies have documented an alarmingly high incidence of this complication when shorter-acting NMBA are used in the operating room. A British investigation reported that 41% of patients receiving intermediate-acting NMBA had TOF ratios < 0.7 on arrival to the PACU. Nearly 2/3 of the subjects in this study received reversal agents prior to tracheal extubation. A similar per-

### Table I.—Incidence of residual neuromuscular block.

<table>
<thead>
<tr>
<th>Study</th>
<th>NMBA administered</th>
<th>Neuromuscular monitoring</th>
<th>Reversal</th>
<th>Definition of residual block</th>
<th>Incidence of residual block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevan et al.⁹</td>
<td>Pancuronium</td>
<td>+/-</td>
<td>+/-</td>
<td>&lt;0.7</td>
<td>17/47 (36%)</td>
</tr>
<tr>
<td></td>
<td>Atracurium</td>
<td>+/-</td>
<td>+/-</td>
<td>&lt;0.8</td>
<td>2/46 (4%)</td>
</tr>
<tr>
<td></td>
<td>Vecuronium</td>
<td></td>
<td></td>
<td></td>
<td>5/57 (9%)</td>
</tr>
<tr>
<td>Hayes et al.¹¹</td>
<td>Vecuronium</td>
<td>+/-</td>
<td>+/-</td>
<td>&lt;0.9</td>
<td>32/50 (64%)</td>
</tr>
<tr>
<td></td>
<td>Atracurium</td>
<td></td>
<td></td>
<td></td>
<td>26/50 (52%)</td>
</tr>
<tr>
<td></td>
<td>Rocuronium</td>
<td></td>
<td></td>
<td></td>
<td>19/48 (59%)</td>
</tr>
<tr>
<td>Baillard et al.¹²</td>
<td>Vecuronium</td>
<td>+/-</td>
<td>+/-</td>
<td>&lt;0.7</td>
<td>239/568 (42%)</td>
</tr>
<tr>
<td>Debaene et al.¹³</td>
<td>Vecuronium</td>
<td>+/-</td>
<td>+/-</td>
<td>&lt;0.7</td>
<td>85/526 (16%)</td>
</tr>
<tr>
<td></td>
<td>Intermediate-acting agents</td>
<td></td>
<td></td>
<td></td>
<td>237/526 (45%)</td>
</tr>
<tr>
<td></td>
<td>Rocuronium</td>
<td></td>
<td></td>
<td></td>
<td>70/274 (25%)</td>
</tr>
<tr>
<td>Kim et al.¹⁴</td>
<td>Vecuronium</td>
<td></td>
<td></td>
<td>&lt;0.9</td>
<td>35/203 (15%)</td>
</tr>
<tr>
<td>Murphy et al.¹⁵</td>
<td>Pancuronium</td>
<td></td>
<td></td>
<td>&lt;0.7</td>
<td>14/35 (40%)</td>
</tr>
<tr>
<td></td>
<td>Rocuronium</td>
<td></td>
<td></td>
<td></td>
<td>2/34 (5.9%)</td>
</tr>
</tbody>
</table>

+: used in all patients; -: used in no patients; +/-: used in some patients and not in others.
percentage of patients (42%) had postoperative TOF ratios <0.7 when a vecuronium neuromuscular block was not reversed before arrival in the PACU. Even a single dose of a NMBA administered prior to tracheal intubation can result in postoperative residual paralysis. Debaene et al. administered a single intubating dose of twice the ED$_{95}$ of an intermediate-acting agent to 526 patients undergoing gynecologic or plastic surgical procedures. Neuromuscular blockade was not reversed. TOF ratios of <0.7 and <0.9 were observed in 16% and 45% of patients in the PACU, respectively. Routine administration of reversal agents does not eliminate the risk of residual paralysis. Kim et al. observed that 25% of patients who received pyridostigmine at the conclusion of the surgical procedure had TOF ratios <0.7 measured immediately after arrival in the PACU.

Most clinical investigations have examined postoperative paralysis in the PACU. TOF ratios were typically quantified 15-30 min after neuromuscular reversal and extubation. Ideally, recovery of neuromuscular function should be assessed prior to tracheal extubation in order to ensure acceptable recovery of respiratory and pharyngeal muscle strength and reduce the risk of respiratory complications. A recent investigation measured TOF ratios immediately prior to tracheal extubation, after clinicians had determined that complete recovery of neuromuscular function had occurred using clinical criteria and standard peripheral nerve stimulators. Management of a rocuronium neuromuscular blockade was carefully monitored and standardized, and reversal agents were administered at a TOF count of ≥2. Immediately prior to tracheal extubation, 58% of patients had TOF ratios <0.7 and 8% had TOF ratios <0.9. Despite the use of a protocol designed to limit the risk of residual paralysis, only a small percentage of patients had achieved acceptable neuromuscular recovery at the time of extubation. These recent clinical investigations demonstrate that impaired neuromuscular recovery is still a common problem in the early recovery period from anesthesia and surgery. During the past decade there has been an increased awareness among clinicians of the hazards of residual neuromuscular block. It is likely that this awareness of the problems associated with residual paresis has resulted in more careful management of NMBAs in the operating room by anesthesia care providers. However, many patients continue to arrive in the PACU with TOF ratios <0.9, despite routine monitoring and reversal of intermediate-acting agents.

**Adverse physiologic effects of residual neuromuscular blockade: volunteer studies**

Several investigations in volunteer subjects have examined the effects of mild degrees of residual block on pharyngeal and respiratory muscle function. Sundman et al. used videomanometry to evaluate pharyngeal muscle function during a partial vecuronium neuromuscular block. Twenty awake volunteers were studied during liquid-contrast bolus swallowing. Pharyngeal function was assessed using fluoroscopy and a manometry pressure catheter. At a TOF ratio of 0.8, impaired coordination of pharyngeal muscle activity was noted in 20% of subjects, and upper esophageal sphincter tone was markedly reduced. In a second study by the same investigators, pharyngeal function was measured in 14 awake volunteers during an infusion of vecuronium titrated to achieve TOF ratios of 0.6-0.8. Using videomanometry of the pharynx and esophagus, the investigators observed misdirected swallowing with aspiration in 4 subjects at a TOF ratio of 0.6 and 3 subjects at a TOF ratio of 0.7. These findings suggest that some patients may be at risk for pharyngeal dysfunction and aspiration during early recovery from anesthesia when incomplete neuromuscular recovery (TOF ratio <0.9) is present.

Eikermann et al. examined the effect of a partial neuromuscular block on pulmonary and upper airway function. Spirometric measurements were obtained during a rocuronium infusion titrated to achieve TOF ratios between 0.5-0.8 in awake subjects. Upper airway obstruction was observed in 2/3 of
the subjects overall, and in 1/3 of the volunteers at a TOF ratio of 0.83. Acceptable recovery of respiratory function did not occur in most of the subjects until recovery of TOF ratios to unity was achieved.

During partial neuromuscular blockade, a normal minute ventilation is maintained by an increase in respiratory rate. Therefore, hypercarbia is usually not present during mild-to-moderate levels of residual paresis. In contrast, small degrees of neuromuscular block can significantly impair the hypoxic ventilatory response. Two studies by Eriksson et al. have examined the effect of a vecuronium infusion on the hypoxic ventilatory response in awake volunteers. At a TOF ratio of 0.7, the ventilatory response to hypoxia was significantly reduced, while the response to hypercapnea was maintained. Animal data suggests that this response is due to a direct effect of NMBA on the carotid body. In rat and rabbit models, the chemosensitivity of the carotid sinus to hypoxia is significantly reduced following the administration of small doses of vecuronium. An inhibition of neuronal nicotinic receptors in the carotid body appears to mediate this effect.

There has been relatively little data published describing the subjective experience of muscle weakness that is present during partial neuromuscular blockade. Kopman et al. administered a mivacurium infusion to 10 awake volunteers; the infusion was adjusted to maintain TOF ratios between 0.65-0.75. Subjects were carefully examined for signs and symptoms of muscle weakness during the infusion and recovery periods. TOF ratios of 0.7-0.75 were associated with visual disturbances, facial weakness, decreased grip strength, an inability to drink through a straw or bite firmly on a tongue blade, difficulty in sitting or speaking, and a generalized sense of weakness. Even at TOF ratios ≥ 0.9, subjects noted visual problems and a generalized fatigue. Few volunteers felt “street ready” until complete recovery of neuromuscular function had occurred.

Volunteer studies demonstrate that minimal levels of residual paralysis (TOF ratios 0.7-0.9) impair pharyngeal muscle function, reduce lower esophageal sphincter tone, increase the risk of aspiration, produce upper airway obstruction, impair the hypoxic ventilatory response, and result in unpleasant symptoms of muscle weakness. It is likely that similar adverse effects are produced in postoperative surgical patients when incomplete neuromuscular recovery is present. The findings from these investigations should be particularly concerning to anesthesiologists, since the volunteer studies were conducted in young, healthy subjects and in the absence of other anesthetic agents. Patients presenting for surgical procedures are typically older than those enrolled in the volunteer studies, and often have multiple coexisting medical conditions. Although unproven, the incidence and risks of residual neuromuscular block are likely increased in an older and sicker surgical patient population. In addition, patients undergoing general anesthesia receive other anesthetic agents (inhalational agents, opioids, benzodiazepines) that may impair respiratory and pharyngeal muscle function. The persistent effects of anesthetic agents in the early postoperative period may compound the adverse impact of residual neuromuscular block on muscle function and increase the risk of complications.

**Adverse physiologic effects of residual neuromuscular blockade: clinical studies in surgical patients**

Several clinical investigations have examined the effect of residual paresis on postoperative recovery of the surgical patient. Murphy et al. randomized 70 patients undergoing major orthopedic surgery to receive pancuronium or rocuronium intraoperatively. Neuromuscular blockade was monitored in the operating room and reversed at the end of the surgical procedure. TOF ratios were measured on arrival to the PACU. Forty percent of the patients receiving pancuronium had TOF ratios <0.7 in the PACU, compared with only 5.9% of the subjects in the rocuronium group. Patients in the pancuronium group had more symptoms of muscle weakness, a higher incidence of postoperative hypoxemia, and delays in meeting PACU discharge criteria and achieving actual discharge. An association between residual neu-
romuscular block (TOF ratio <0.9) and both postoperative hypoxemia and prolonged PACU admission times was noted.

Many clinicians continue to use pancuronium for cardiac surgical procedures. A recent survey of cardiac anesthesiologists in the United States revealed that nearly 2/3 of respondents used long-acting NMBAs in patients undergoing cardiopulmonary bypass. In addition, respondents noted that neuromuscular block was rarely monitored and infrequently reversed at the conclusion of procedures. Residual paralysis is not perceived to be a problem in this patient population, since most patients remain intubated for 4-12 h postoperatively. Clinical trials have assessed the impact of residual paralysis on recovery of the cardiac surgical patient. Murphy et al. randomized 110 patients undergoing elective coronary artery bypass graft surgery or single valvular surgery to receive pancuronium or rocuronium. Neuromuscular block was monitored but not reversed. Significant increases in the duration of weaning of ventilatory support and of tracheal intubation were observed in patients administered pancuronium. On average, patients in the pancuronium group remained intubated for 2.5 h longer than those in the rocuronium group. In a subsequent investigation, the same authors quantified recovery of neuromuscular function in 82 fast-track cardiac surgical patients administered pancuronium or rocuronium. TOF ratios were measured using acceleromyography in the postoperative unit until a TOF ratio ≥0.9 was achieved. Median times to achieve this endpoint were nearly twice as long in the pancuronium group (7 h, 52 min) compared to the rocuronium group (3 h, 38 min). Extubation was delayed due to residual neuromuscular block in 7 of 10 patients in the pancuronium group and in no patients in the rocuronium group.

Residual neuromuscular block can produce hypoxemia in surgical patients through several potential mechanisms, which include an effect on respiratory muscle function, a reduction in upper airway muscle tone, or a direct effect on the hypoxic ventilatory drive. Bissinger et al. performed an investigation to determine whether residual neuromuscular block following the use of pancuronium or vecuronium was associated with hypoxemia in the PACU. TOF ratios were quantified on arrival to the PACU with acceleromyography. In the pancuronium group, 60% of the patients with TOF ratios <0.7 had episodes of postoperative hypoxemia, compared to only 10% of the patients with TOF ratios ≥0.7. An association between residual paresis and postoperative hypoxemia has also been noted in patients following major orthopedic surgery.

In 1997, a large-scale Scandinavian study was published which was designed to assess the impact of residual neuromuscular block on the incidence of postoperative pulmonary complications. A total of 691 patients undergoing a variety of surgical procedures were randomized to receive pancuronium, vecuronium, or atracurium. Neuromuscular monitoring and reversal were routinely used, and TOF ratios were measured mechanomyographically in the PACU. Patients were examined for 6 days for evidence of pulmonary complications (pneumonia and/or atelectasis). In the pancuronium group, the incidence of pulmonary complications was 3 times higher in patients with TOF ratios <0.7 (16.9%) compared to patients with TOF ratios ≥0.7 (4.8%). Multiple regression analysis identified a TOF ratio of <0.7 following the use of pancuronium as a risk factor for postoperative pulmonary complications.

The data from volunteer studies and clinical trials in surgical patients provides strong evi-
evidence that impaired neuromuscular function in the early period following anesthesia and surgery can adversely affect postoperative recovery (Table II). Pharyngeal and respiratory muscle dysfunction is present during minimal levels of neuromuscular block. Impaired function of these muscle groups may ultimately result in postoperative hypoxemia and pulmonary complications. Postoperative residual paralysis may also affect other muscle groups, resulting in signs and symptoms of muscle weakness in awake patients, delays in meeting discharge criteria, and prolonged postoperative intubation times. The impact of residual paresis on major morbidity and mortality is less certain, however. At the present time, only one investigation has examined the relationship between residual neuromuscular block and major morbidity (pulmonary complications) following general anesthesia. Additional large-scale clinical trials are required to determine whether muscle weakness resulting from NMBAs significantly impacts important postoperative outcomes or death.

### Assessment of residual neuromuscular block

**Clinical evaluation**

The traditional examination performed in the operating room to detect residual paresis is the 5-s head lift. Data has demonstrated that when a 5-s head lift is sustained, most subjects had acceptable values for vital capacity and maximal voluntary ventilation. Ali et al. observed that no patients with a TOF ratio <0.4 were able to sustain a 3-s head lift, while all patients with a TOF ratio >0.6 could perform this task. In other investigations, 9 of 10 patients could sustain a 5-s head lift at a TOF ratio of 0.7, and 23 of 23 patients could maintain a head lift for 5 s when TOF ratios had recovered to 0.8. In contrast, other studies have demonstrated that some subjects can perform a 5-s head lift with TOF values as low as 0.25-0.4. In a recent investigation in volunteers, all subjects except one could sustain a head lift for more than 5 s at a TOF ratio of 0.5. Thus, the demonstration of a 5-s head lift does exclude the presence of residual neuromuscular block. Significant muscle weakness (TOF values as low as 0.25) may be present in some patients who are able to perform this test.

Maximum inspiratory force (MIF, negative pressure generated against an occluded airway) has been used as a measure of return of muscle strength in patients emerging from general anesthesia. A value of -25 to -30 cm H₂O has been accepted as a criteria for adequate neuromuscular recovery. However, in an awake volunteer study during partial paralysis, no subjects were able to maintain a patent airway at a MIF of -25 cm H₂O. The ability to swallow and hand grip strength were also abolished at a MIF of -25 cm H₂O. Recent data has shown that significant impairment of maximum inspiratory flow occurs at a TOF ratio of 0.8. Therefore, MIF appears to be a poor test in predicting recovery of muscle strength and in determining the ability to maintain a patent airway following tracheal extubation.

**Standard peripheral nerve stimulator**

Small, portable peripheral nerve stimulators are now commonly used in the operating room setting. Neuromuscular monitoring with a standard peripheral nerve stimulator allows the clinician to avoid excessive administration of NMBAs, determine whether blockade can be reversed at the conclusion of surgery, and

---

**Table II.**—Adverse effects of residual neuromuscular block.

<table>
<thead>
<tr>
<th>Volunteer studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired pharyngeal function</td>
</tr>
<tr>
<td>Increased risk of aspiration</td>
</tr>
<tr>
<td>Upper airway obstruction</td>
</tr>
<tr>
<td>Impaired hypoxic ventilatory drive</td>
</tr>
<tr>
<td>Profound symptoms of muscle weakness</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical studies in surgical patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delays in meeting PACU discharge criteria and achieving actual discharge</td>
</tr>
<tr>
<td>Symptoms and signs of profound muscle weakness</td>
</tr>
<tr>
<td>Increased risk of postoperative hypoxemia</td>
</tr>
<tr>
<td>Prolonged postoperative intubation times (cardiac surgical patients)</td>
</tr>
<tr>
<td>Increased risk of postoperative respiratory complications</td>
</tr>
</tbody>
</table>

### TABLE II. — Adverse effects of residual neuromuscular block.

- Impaired pharyngeal function
- Increased risk of aspiration
- Upper airway obstruction
- Impaired hypoxic ventilatory drive
- Profound symptoms of muscle weakness

**Clinical studies in surgical patients**

- Delays in meeting PACU discharge criteria and achieving actual discharge
- Symptoms and signs of profound muscle weakness
- Increased risk of postoperative hypoxemia
- Prolonged postoperative intubation times (cardiac surgical patients)
- Increased risk of postoperative respiratory complications

---

102 MINERVA ANESTESIOLOGICA Marzo 2006
Residual Neuromuscular Blockade: Incidence, Assessment, and Relevance in the Postoperative Period

Murphy

assess recovery of neuromuscular function prior to tracheal extubation. The ulnar nerve at the wrist is the most popular site for neuromuscular blockade assessment, and contraction of the muscles around the eye is evaluated. Several patterns of nerve stimulation are used by anesthesiologists, which include:

1) Single twitch: a single supramaximal stimulus is applied for 0.1-0.3 ms. Twitch height will begin to decrease when 75% of the nicotinic acetylcholine receptors are blocked and will disappear when 90-95% of the receptors are occupied. Routine clinical assessment of residual block is difficult with single twitch stimulation, since twitch height must be compared to baseline values (control twitch height must be measured before administration of NMBAs).

2) TOF: TOF stimulation is the most frequently used pattern of neurostimulation in the perioperative setting. Four supramaximal stimuli are applied to a nerve over a 2-s interval, and the number of responses observed. The TOF count is simple to perform and does not require a control twitch height. When 70-75% of the nicotinic acetylcholine receptors are blocked, the forth response (T4) is decreased. The T3, T2, and T1 responses are abolished when 85%, 85-90%, and 90-98% of the nicotinic acetylcholine receptors are occupied, respectively.

3) Tetanic stimulation and post-tetanic count: stimulation of motor nerves at frequencies >30 Hz results in fusion of twitch responses and sustained muscle contraction. Fade (decrease in muscle response to rapid stimulation) is observed during tetanic stimulation when more than 70-75% of the nicotinic acetylcholine receptors are blocked. The degree of fade can be used to estimate the intensity of neuromuscular blockade. When a single twitch stimulus is applied within 2 min of a tetanic stimulus, an enhanced response occurs as a result of post-tetanic potentiation. A post-tetanic count is performed by applying supramaximal stimuli once every second following a 5-s 50 Hz tetanic stimulus. The post-tetanic count can be used to assess deep neuromuscular blockade and to estimate time to recover twitches when no response to TOF stimulation is present.

4) Double-burst stimulation (DBS): DBS involves the application of 2 short bursts of tetanic stimuli (50 Hz) separated by a 750 ms interval. Each burst consists of a series of 3 and 2 impulses (DBS3,2) or 3 and 3 impulses (DBS3,3). DBS was developed to allow clinicians to more accurately assess small degrees of residual paresis using visual or tactile observations.

Several studies have examined the ability of clinicians to detect residual neuromuscular blockade using standard peripheral nerve stimulators. Visual and tactile evaluation of fade in response to nerve stimulation is difficult to observe during subtle neuromuscular block. Experienced clinicians are unable to reliably detect fade in response to TOF stimulation unless TOF ratios are <0.4. In another clinical investigation, 48% of patients with no evidence of fade during TOF stimulation had TOF ratios <0.6. Manual assessment of evoked responses to DBS appears to be a more sensitive method of neuromuscular monitoring than TOF stimulation; fade is more reliably detected up to a TOF value of 0.6. However, the absence of fade during manual evaluation of responses to DBS does not exclude residual paresis, since TOF ratios of 0.6-1.0 cannot be consistently detected. The use of tetanic stimulation does not appear to improve the clinicians ability to observe fade over TOF or DBS techniques.

Quantitative neuromuscular monitoring

As described previously, small degrees of residual paresis (TOF ratios 0.7-0.9) can potentially impair clinical recovery following general anesthesia. Standard clinical evaluations and peripheral nerve stimulators are insensitive tests for determining whether full recovery of neuromuscular function has occurred at the conclusion of the surgical procedure (Table III). Quantitative neuromuscular monitoring was developed in order to allow clinicians to accurately measure single twitch height and TOF ratio values.
methods of recording evoked responses are available:

1) Mechanomyography: mechanomyography measures the mechanical force of a muscle contraction. Isometric contraction of the adductor pollicis is quantified following ulnar nerve stimulation. Mechanomyography is considered the gold standard method of assessing evoked responses. However, since the equipment is bulky and difficult to set up and use, mechanomyography is rarely used in clinical practice.

2) Electromyography (EMG): EMG measures the electrical activity (compound muscle action potentials) of the stimulated muscle. Typically, EMG responses are measured with electrodes at the thenar eminence, the hypothenar eminence, or the first dorsal interosseous muscles of the hand. Evoked responses measured with EMG correlate well with responses recorded with mechanomyography. The EMG signal can be adversely affected by a number of factors, which include electrical interference, improper electrode placement, hypothermia, and direct muscle stimulation. Due to these limitations, EMG is rarely used in the operating room setting.

3) Acceleromyography: mechanomyography and electromyography are utilized primarily as research tools. Acceleromyography technology was developed for routine clinical use in the operating room, PACU, and ICU. Acceleromyography devices are small, portable, and relatively easy to set up and use. Acceleromyography is based on Newton’s second law which states that force = mass x acceleration. If mass is constant, force can be calculated by measuring acceleration. Acceleration of the stimulated muscle is quantified using a small piezoelectric crystal embedded in a transducer. A small electrical signal is generated in the transducer during movement of a muscle, which is amplified and displayed on the device. Since no preload is required on the stimulated muscle, additional monitoring sites can be used (muscles surrounding the eyes). (Figure 1).

Several investigations have demonstrated a good correlation between TOF values obtained with acceleromyography and mechanomyography. However, recent studies suggest that acceleromyography may underestimate TOF ratios during recovery.

---

**TABLE III**—Methods to assess residual neuromuscular block.

<table>
<thead>
<tr>
<th>Clinical evaluation</th>
<th>Increasing sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable minute ventilation</td>
<td></td>
</tr>
<tr>
<td>Five-second hand grip</td>
<td></td>
</tr>
<tr>
<td>Maximum inspiratory force &gt;30 cm H2O</td>
<td></td>
</tr>
<tr>
<td>Head lift &gt;5 s</td>
<td></td>
</tr>
<tr>
<td>Head lift &gt;10 s</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peripheral nerve stimulation</th>
<th>Increasing sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual/tactile assessment fade-single twitch</td>
<td></td>
</tr>
<tr>
<td>Visual/tactile assessment fade-tetanus (5 s)</td>
<td></td>
</tr>
<tr>
<td>Visual/tactile assessment fade-DBS</td>
<td></td>
</tr>
<tr>
<td>Quantitative monitoring-acceleromyography</td>
<td></td>
</tr>
<tr>
<td>Quantitative monitoring-electromyography</td>
<td></td>
</tr>
<tr>
<td>Quantitative monitoring-mechanomyography</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1**—A commercially produced acceleromyography device (the TOF-Watch). Stimulation electrodes are placed over the ulnar nerve and the transducer is attached to the thumb to measure the evoked responses.
from neuromuscular blockade (when compared to the gold standard mechanomyography). Control TOF values are consistently greater than 1 (approximately 1.1 to 1.15) when measured with acceleromyography.\textsuperscript{42, 43} A control TOF ratio greater than 1 may influence subsequently measured TOF values (acceleromyography measurements are higher than those recorded by mechanomyography). Capron et al. observed that an acceleromyographic TOF ratio 0.97 corresponded to a mechanomyographic TOF ratio of 0.9.\textsuperscript{43} The authors conclude that acceleromyography may underestimate the true incidence of residual paresis, and that TOF ratios must recover to 1 (rather than 0.9) to reliably exclude residual block.

Methods to reduce the risks of residual neuromuscular blockade

The risks of residual paresis can be minimized by careful management of neuromuscular blockade in the intraoperative period. There are several well-known methods that can be easily applied by clinicians to reduce the incidence of postoperative muscle weakness. These include the following:

1) Avoidance of long-acting NMBAs: several clinical trials have compared the risk of postoperative residual neuromuscular block following the use of long- and intermediate-acting NMBAs in the operating room. These studies have shown that the incidence of residual paresis is 3-4 times higher in patients receiving long-acting agents like pancuronium.\textsuperscript{8-10} Long-acting NMBAs are now rarely used in adult patients unless prolonged postoperative tracheal intubation is anticipated.

2) Use of routine neuromuscular monitoring in the operating room: monitoring of the depth of neuromuscular blockade during the surgical procedure with standard peripheral nerve stimulators or acceleromyography devices may reduce the risk of incomplete neuromuscular recovery (Table IV).\textsuperscript{31, 44-47} Shorten et al. examined whether standard TOF monitoring (tactile assessment of the TOF count) influenced the occurrence of residual block in the PACU.\textsuperscript{41} Patients were randomized to receive either TOF monitoring in the operating room or no intraoperative neuromuscular monitoring. TOF ratios were quantified with electromyography on arrival to the PACU. Fifteen percent of patients in the monitoring group had TOF ratios <0.7 in the PACU, compared to 47% of subjects who had no intraoperative monitoring. The incidence and degree of residual block can also be decreased if DBS monitoring is used intraoperatively. The routine application of DBS monitoring resulted in significantly fewer patients (24%) exhibiting TOF ratios <0.7 in the PACU compared to a group managed with no neuromuscular monitoring (57%).\textsuperscript{31}

3) Acceleromyography monitoring during the surgical procedure and prior to tracheal extubation may have a beneficial impact on the incidence of residual paresis. Two studies randomized patients to either a group monitored with acceleromyography or to a control group (no neuromuscular monitoring).\textsuperscript{46, 47} TOF ratios were quantified with mechanomyography immediately after tracheal extubation. Both investigations demonstrated that significantly fewer patients monitored with acceleromyography had TOF ratios <0.7-0.8, and that signs of postoperative muscle weakness were less frequent in this group. However, the time from the end of the surgical procedure to tracheal extubation was longer (2.5-5 min) in the acceleromyography group. In summary, neuromuscular monitoring may play a role in attenuating the severity of residual paresis in patients during recovery from anesthesia and surgery. Acceleromyography is a more sensitive tool for detecting residual neuromuscular block than standard peripheral nerve stimulators; commercially available acceleromyography devices should be used prior to tracheal extubation if significant muscle weakness is suspected.

4) Avoidance of total twitch suppression: reversal of neuromuscular blockade should not be attempted until spontaneous recovery of neuromuscular function has occurred (at least 1 response to TOF stimulation). The risk of intense neuromuscular block at the conclusion of the surgical procedure is increased if a TOF count of 0 is maintained intraoperatively. Fortunately, profound muscle relaxation
is rarely required in the operating room. A TOF count of 0 should be maintained during a surgical procedure only if patient movement or coughing could result in serious injury (i.e., during ophthalmic surgery on an open globe or during procedures on patients with critically elevated intracranial pressure). Adequate surgical relaxation (abdominal surgery) is usually present at a TOF count of 1-2.

5) Routine reversal of NMBAs: reversal of neuromuscular blockade is not without risks. Anticholinesterase agents produce a number of adverse effects, which include bradycardia, nausea and vomiting, and bronchoconstriction. Some clinicians believe that the risks associated with anticholinesterase administration outweigh the potential benefits, and only use reversal agents when obvious muscle weakness is present. This practice of avoiding (or selectively using) anticholinesterases increases the risk of postoperative paralysis. Debaene et al. examined residual neuromuscular block in the PACU in patients that had received a single intubating dose of an intermediate-acting NMBA. Neuromuscular block was not reversed in the 528 patients studied. On arrival to the PACU, TOF ratios <0.7 and <0.9 were present in 16% and 45% of the patients, respectively. In nearly half of the patients, more than 2 h had elapsed between NMBA administration and TOF measurements. The authors conclude that a long duration between last NMBA dosing and the conclusion of the surgical procedure does not guarantee acceptable recovery of muscle strength. Due to the unpredictable nature of spontaneous neuromuscular recovery, clinicians should routinely reverse the effects of NMBAs (unless complete recovery of TOF ratios has been documented with acceleromyography).

6) Reversal of neuromuscular blockade at a TOF count of 2-3: the time required to achieve full neuromuscular recovery is dependent upon the extent of spontaneous recovery when the block is reversed with anticholinesterases. Reversal time is shortened when at least 2 responses to TOF stimulation are observed, and more rapid when a TOF count of 3-4 is present. The reversal time for an intense neuromuscular block is typically 20-30 min (TOF count of 1 to a TOF ratio of 0.7). In contrast, a mild neuromuscular block (TOF count of 2-4) can often be reversed within 3-6 min. When long-acting NMBAs are used, anticholinesterase agents should not be administered until at least 1 response to TOF stimulation is present. Recent data suggests that reversal of profound rocuronium or vecuronium blockade need not be delayed until spontaneous recovery has occurred. Bevan et al. randomized 80 adult patients to receive 0.07 mg/kg of neostigmine at 1 of 4 different time points; 5 min after rocuronium of vecuronium administration, or at a first twitch recovery of 1%, 10%, or 25%. The times from NMBA administration to a TOF ratio of 0.7 were similar in

### Table IV. Impact of neuromuscular monitoring on the incidence of residual paresis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of monitoring</th>
<th>NMB used</th>
<th>Effect of monitoring on dose of NMB used</th>
<th>Number of patients with residual neuromuscular block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shorten et al.</td>
<td>Manual assessment of TOF</td>
<td>Pancuronium</td>
<td>None</td>
<td>No monitoring 9/19 (47%)</td>
</tr>
<tr>
<td>Pedersen et al.</td>
<td>Manual assessment of TOF</td>
<td>Pancuronium</td>
<td>None</td>
<td>No monitoring 15/40 (38%)</td>
</tr>
<tr>
<td>Fruegaard et al.</td>
<td>Manual assessment of DBS</td>
<td>Pancuronium</td>
<td>None</td>
<td>No monitoring 17/30 (57%)</td>
</tr>
<tr>
<td>Mortensen et al.</td>
<td>Acceleromyography measurement of TOF</td>
<td>Pancuronium</td>
<td>None</td>
<td>No monitoring 11/21 (52%)</td>
</tr>
<tr>
<td>Gatke et al.</td>
<td>Acceleromyography measurement of TOF</td>
<td>Rocuronium</td>
<td>None</td>
<td>No monitoring 10/120 (16.7%)</td>
</tr>
</tbody>
</table>

TOF: train-of-four; DBS: double burst stimulation; NMBA: neuromuscular blocking agent.
all groups and independent of the timing of neostigmine administration.

7) Early antagonism of neuromuscular blockade: clinicians frequently administer anticholinesterases when surgical dressings are being applied at the end of the procedure. Since full reversal of more intense levels of neuromuscular block may require up to 20-30 min, anticholinesterases should be used at least 15-30 before the anticipated time of tracheal extubation. Antagonism of NMBAs should be initiated when muscle relaxation is no longer needed instead of at the conclusion of skin closure. Even when neostigmine is administered at a TOF count of 4 at the end of the procedure, up to 1/3 of patients may have TOF ratios <0.9 20 min later.17

Adherence to strict protocols guiding the management of neuromuscular blockade will reduce, but not eliminate, the problem of residual paralysis. Kopman et al. designed an investigation to determine if experienced clinicians, using careful intraoperative dosing and monitoring of NMBAs, could reduce the incidence of postoperative paralysis.51 Patients were randomized to receive either pancuronium or mivacurium. A TOF count of at least 1 was maintained during the operation. Reversal agents were only administered when spontaneous recovery to a TOF count of 2 was present, and sufficient time was allowed between reversal and extubation. The mean TOF ratio on arrival to the PACU was 0.93 in the mivacurium group and 0.86 in the pancuronium group. Only 2 of 56 patients in the pancuronium group had TOF ratios <0.7 in the PACU. These findings suggest that careful intraoperative management of NMBAs and reversal agents can have a beneficial effect on the occurrence of residual paresis. However, complete recovery of neuromuscular function may be difficult to achieve when long-acting NMBAs are used; only 19 of 56 patients in the pancuronium had TOF ratios ≥0.9 30 min postreversal.

Conclusions

Residual neuromuscular blockade is frequently observed during the early recovery period from general anesthesia. Despite the common clinical practice of using intermediate-acting NMBAs in the operating room, many patients continue to arrive in the PACU with evidence of incomplete neuromuscular recovery. Small degrees of residual paresis can produce a variety of adverse physiologic effects, which include upper airway obstruction, impaired airway protective reflexes, a reduced hypoxic ventilatory drive, and unpleasant symptoms and signs of muscle weakness. Investigations in postoperative surgical patients suggest that residual neuromuscular block can impair clinical recovery and may be associated with increased morbidity. The risks of residual paralysis can be reduced, but not eliminated, by careful intraoperative dosing, monitoring, and reversal of NMBAs.
References


