Peripheral Nerve Stimulators
Physical principles and clinical applications

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Peripheral Nerve Stimulators (PNS) are used to:

Monitor neuromuscular blockade
- During induction of anaesthesia for intubation
- During surgery to guide repeated doses of muscle relaxants to assess the depth of relaxation
- To differentiate between different types of block
- At the end of surgery to assess the ability of reversal
- At the end of anaesthesia or in recovery to assess the degree of residual blockade

Peripheral nerve identification
- To help identify peripheral nerves for nerve mapping
- To help identify peripheral nerves for nerve blockade
- To help prevent intraneural nerve injection of local anaesthetic

An understanding of neuromuscular junction electrophysiology is vital to understanding the clinical application of PNS.

Why is monitoring so important?
Undetected Residual neuromuscular block is common in the recovery room. Up to 42% of patients receiving intermediate acting non-depolarising muscle relaxants arrive in with a TOF ratio of less than 0.7. Standard clinical criteria do not reliably detect residual blockade and standard of care has shifted the accepted TOF ratio to 0.9 or greater. Residual neuromuscular blockade contributes to greater adverse respiratory events, greater chance of re-intubation, longer recovery stay and ICU admission.

Properties of an electrical nerve stimulator
The PNS generates a standard electrical pulse, which should be Supramaximal – A supramaximal stimulus is a stimulus that is greater than that needed to activate all the nerve fibres in a nerve. A stimulus of 20-25% more than that needed to generate a maximal clinical response is usually used. Electric stimulation is the most commonly used but theoretically magnetic can also be used.

Constant current not voltage generator
A current setting of 60 MA will achieve supramaximal stimulation in most cases. The level of current passing through the nerve between electrodes, not the voltage, achieves nerve stimulation. The resistance in the patients skin is influenced by:
- Electrode gel dries or makes poor contact
- The patient’s level of expiration changes
- Changes in patient body temperature – resistance increases as the skin temp cools
Current delivered by constant current stimulators remains the same even when the patient’s resistance changes compared to constant voltage stimulators, thus ensuring supramaximal stimulation. Current output should be limited to less than 80 mA to prevent tissue damage. The *Rheobase* is the minimal current required to stimulate the nerve with a long pulse.

### Monophasic rectangular waveform
Monophasic and rectangular waveforms are essential to prevent multiple nerve stimulations. Assuming a square pulse of the current is used to stimulate the nerve, the total energy (charge) applied to the nerve is a product of the intensity of the current and the duration of the pulse.

### Duration of stimulus
Chronaxy is the property whereby a current must flow for a minimum time before the nerve tissue will depolarise no matter how high the current may be. The chronaxy time is about 80 μsec in mammalian motor nerve.

The chronaxy can be used as a measure of the threshold for any particular nerve and it is useful when comparing different nerves or nerve fibre types. Certain nerves have a different chronaxie based on their physical properties (myelination, size, etc). Also, certain patient conditions, such as diabetes, have an effect on chronaxy.

### Safety and ergonomic features
- Portability
- Warning when the set current is not delivered
- Display of polarity – so that the negative electrode can be placed distally for maximal response.
- Different stimulus patterns available
- Default to lower current options when attached to needle electrodes or a stimulating needle

### Placement of Electrodes:
The electrodes should be placed over the path of the peripheral nerve. The negative (black) electrode is the activating stimulating electrode, and the most effective stimulation is obtained when placed closest to the muscle terminus. The positive electrode (red) is placed 2 cm proximally.

Common sites for placement appear below:

<table>
<thead>
<tr>
<th>DIAGRAM</th>
<th>NOTES</th>
</tr>
</thead>
</table>
| ![Nerve: Ulnar nerve](image) | **Nerve:** Ulnar nerve  
**Muscle:** Adductor pollicis  
**Action:** Thumb adduction  
**Black:** 1-2 cm proximal to wrist crease  
**Red:** 2-3 cm proximal to black |
| ![Nerve: Facial nerve](image) | **Nerve:** Facial nerve  
**Muscle:** Orbicularis oculi and Corrugator supercilii  
**Action:** Twitching of eyelid and eyebrow  
**Black:** Just anterior to tragus  
**Red:** Lateral to outer canthus of eye |
| ![Nerve: Posterior tibial nerve](image) | **Nerve:** Posterior tibial nerve (sural nerve)  
**Muscle:** Flexor hallucis brevis  
**Action:** Plantar flexion of great toe  
**Black:** Over posterior aspect of medial malleolus, over posterior tibial artery  
**Red:** 2-3 cm proximal to black |
2 sites are commonly used to establish the depth of paralysis. Measurement at the adductor pollicis correlates well with the tone in the upper airway and upper oesophageal muscles. The muscles around the eye (orbicularis oculi and corrugator supercilii) recover early (similar to the diaphragm) and a TOF of 4 here is often correlated with a TOFC of 2 or less at the adductor pollicis.

Patterns of stimulation

Single twitch
An electrical pulse is delivered at 1Hz, and the ratio of the evoked twitch compared with that before muscle relaxation gives an indication of neuromuscular blockade. When 75% of the post junctional Ach receptors are occupied by NMBA, twitch magnitude starts to decrease. When there is 100% occupation, no twitch is elicited.

Useful for monitoring of post junctional receptor, as for deep relaxation required for intubation.

Train of four
Four pulses are given at a frequency of 2Hz or 0.5 seconds apart, potentially eliciting 4 twitches (T1-T4). The ratio of the first to the last (T1:T4) indicates the degree of neuromuscular block. Non depolarising neuromuscular blocking agents (NMBA) occupy receptors producing a decrease in magnitude of the first twitch compared with a pre relaxant stimulus and a progressive decrease in magnitude of T1 compared to T4 (Fade). At 75% occupancy T4 disappears. Similarly at 80, 90 and 100% occupancy T3, T2 and T1 disappear. With recovery the twitches reappear in reverse order.

TOF ratio is the ratio of T1 vs. T4

TOF count is a numerical count of twitches elicited with a TOF stimulus

Clinically accepted values for TOF count:
1 twitch for intubation
1-2 twitches during anaesthesia
3-4 twitches before reversal of neuromuscular blockade

Double Burst Stimulation (DBS)
This consists of 2 bursts of 3 stimuli at 50 Hz with each triple burst separated by 750 ms. These appear visually as 2 separate stimuli T1 and T2, and the ratio of these is related to the TOF ratio. It is used as it is easier for the operator to interpret reliably compared to comparing the T1:T4 ratio visually.

Tetanic stimulation
The impulse at 50 Hz of 5 ms produces detectable Fade in muscle contraction, the extent of which is related to the neuromuscular block. No fade indicates no neuromuscular block. In intense neuromuscular block, TOF stimulation may elicit no twitches. Tetanic stimulation causes post-tetanic facilitation (PTP) to mobilize presynaptic Ach. Subsequent 1 Hz twitches can now overcome the high concentration of NMBA’s. The number of twitches generated (i.e. the post tetanic count) reflects the degree of neuromuscular blockade.
Depolarising NMBA’s react differently to the PNS modes of stimulation. They produce equal but reduced twitches in response to single twitch and TOF stimulation (the T4:T1 ratio is 1) reduced but sustained contraction with tetanic stimulation. They do not demonstrate either tetanic fade or PTP.

**How do we monitor the effect of the stimulus?**

The muscle response can be assessed by visual and tactile methods – these are the easiest, but can often be unreliable and inaccurate. Objective measurement of neuromuscular monitoring is the only way of accurately assessing residual neuromuscular blockade. It is conducted via quantitative measurement of the strength of contraction of a peripheral muscle in response to peripheral nerve stimulation produced by 2 stimulating electrodes. Each measurement technique measures the force of contraction either directly or by a factor proportional to that force.

**Electromyography** uses electrodes to record the evoked electrical response of the muscle. Stimulating electrodes are placed over the nerve and recording electrodes over the muscle being stimulated. Stimulation of the nerve results in depolarisation of the muscle and the amplitude of the compound muscle action potential is recorded and expressed as a percentage of control or as a TOF ratio. Typically the ulnar nerve is used and the electrodes are placed over the muscle of adductor pollicis. This is easily accessible but a drawback is that small movements of the hand may affect the response, as may electro cautery.

**Mechanomyography** uses electrodes to measure the evoked muscle response of a muscle. A small weight is suspended from the muscle to maintain isometric contraction. The tension produced on PNS is converted into an electrical signal. This gold standard is very accurate, but is difficult to set up in practice and is used mainly in research.

**Acceleromyography** uses Newton’s second law of motion. Force equals mass times acceleration. The transducer uses a piezoelectric crystal secured to the distal part of the digit (thumb) being measured and the PNS provides the electrical stimulus (ulnar nerve). Acceleration of the distal digit is directly proportional to the force of the contraction (mass stays the same) and therefore inversely proportional to the degree of NMB.

**Kinemyography** uses a piezoelectric polymer sensor in the groove between the thumb and the index finger. Movement of the muscle generates a voltage in the sensor which can be measured. This is not commonly used.

**Phonomyography** uses a high fidelity narrow bandwidth microphone placed along side the muscle, and measure sound intensity. This is not commonly used.

**Clinical evaluation of responses after administration of depolarising NMBA’s**

**Phase 1 Block**
- Patients with normal plasma cholinesterase activity who receive a moderate dose of succinylcholine (0.5-1.5mg/kg).
- There is no fade during tetanic stimulation or TOF
- No PTP

**Phase 2 Block**
- Patients who have abnormal cholinesterase activity, who have had prolonged exposure to depolarising agents.
- Also known as mixed or dual type block, they display characteristics of non-depolarising block, i.e. fade in response to TOF or tetanic stimulation and PTP.

**Clinical evaluation of responses after administering a non-depolarising NMBA**

Injection of a dose of depolarising muscle relaxant to allow intubation, results in 3 levels of neuromuscular blockade (NMB), Intense blockade, moderate or surgical blockade and recovery. Different muscle groups require display degrees of relaxation during surgery and recovery, e.g. intubation requires intense NMB or abdominal wall relaxation moderate NMB for surgery.
Intense NMB
Time to intubating dose depends on the drug and dose administered. There will be no repose to single twitch or TOF. The duration of this period is dependant on patient and drug factors. The PTC can be used to predict the appearance of the first twitch during this period. Clinically this may be applicable where a large dose of muscle relaxant is given and the case is subsequently cancelled.

Moderate or Surgical Blockade
This begins with the appearance of T1 and ends when T4 appears.

Recovery
The recovery phase starts once T4 appears i.e. less than 75 percent of receptor sites are occupied by NMBA. When the TOF ratio is greater than 0.4 it becomes very difficult to assess the presence of fade without objective monitoring. The DBS may help in this situation.

Different muscle groups recover at different rates, which may have clinical implications in evaluating residual weakness after administration of NMBA.

<table>
<thead>
<tr>
<th>Depth of Block</th>
<th>Posttetanic Count</th>
<th>Train-of-Four Count</th>
<th>Subjective Train-of-Four Ratio</th>
<th>Measured Train-of-Four Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intense (profound) block</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Deep block</td>
<td>≥1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Moderate block</td>
<td>NA</td>
<td>1-3</td>
<td>Fade present</td>
<td>0.1-0.4</td>
</tr>
<tr>
<td>Light (shallow) block</td>
<td>NA</td>
<td>4</td>
<td>No fade</td>
<td>&gt; 0.4 but &lt; 0.90</td>
</tr>
<tr>
<td>Minimal block (near recovery)</td>
<td>NA</td>
<td>4</td>
<td>No fade</td>
<td>≥ 0.90-1.0</td>
</tr>
<tr>
<td>Full recovery (normal function)</td>
<td>NA</td>
<td>4</td>
<td>No fade</td>
<td></td>
</tr>
</tbody>
</table>

NA = not applicable
What TOF ratio indicates recovery from NMBA?
Previously a TOF ratio of 0.7 was thought to be adequate for sufficient recovery in the postoperative period.

This correlates with clinical signs as below:

*Clinical tests of postoperative muscular recovery*

<table>
<thead>
<tr>
<th>Unreliable</th>
<th>Reliable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained eye opening</td>
<td>Sustained head-lift for 5 seconds</td>
</tr>
<tr>
<td>Protrusion of the tongue</td>
<td>Sustained leg lift for 5 seconds</td>
</tr>
<tr>
<td>Arm lift to opposite shoulder</td>
<td>Sustained hand grip for 5 seconds</td>
</tr>
<tr>
<td>Normal tidal volume</td>
<td>Sustained “tongue depressor test”</td>
</tr>
<tr>
<td>Normal or near normal vital capacity</td>
<td>Maximum inspiratory pressure &gt;40-50 cm H₂O</td>
</tr>
<tr>
<td>Maximum inspiratory pressure &lt;40-50 cm H₂O</td>
<td>(Normal swallowing?)</td>
</tr>
</tbody>
</table>

- TOF ratios below 0.7 are a significant risk factor for postoperative pulmonary complications.
- TOF ratios of between 0.7-0.9 decrease chemoreceptor sensitivity to hypoxia
- TOF ratios of less than 0.9 are associated with increased risk of regurgitation and aspiration, diplopia, and subjective feelings of weakness.

*Residual neuromuscular blockade* is inadequate neuromuscular recovery as measured by objective neuromuscular monitoring which may show a TOF ratio of less than 0.9

What Nerve Stimulator mode to use when?

? = TOF is less useful in the recovery area unless some form of objective monitoring is used

**Applicability with Sugammadex**

Sugammadex is a modified gammadycyclodextrin that binds aminosteroid NMB’s (rocuronium > vecuronium > pancuronium). Because of the 1:1 molar ratio between sugammadex and the aminosteroid NMBA, there has to be sufficient sugamadex molecules administered to encapsulate ALL the free molecules of the NMBA. The TOFC may be useful to determine the most appropriate dose to ensure full reversal. At a TOFC count of 1-3, a dose of 2 mg/kg will reliably produce TOF>0.9 in 2 minutes. For reversal of deep blockade (PTC >1), a dose of 4 mg/kg is recommended. For Profound block (PTC=0), a dose of 16mg /kg is recommended.

**Key points:**
- Clinical evaluation of recovery of neuromuscular function has limitations.
- Residual neuromuscular weakness has significant morbidity.
- Absence of fade does not exclude significant residual block.
- Objective neuromuscular monitoring is important.
- Clinically significant residual neuromuscular blockade is less likely if the TOF ratio (as measured objectively) is greater than 0.9.
Learning Questions:

Which of the following is the most reliable pattern to determine residual neuromuscular blockade?

a) TOF <0.7  
b) TOF <0.9  
c) Clinical signs  
d) No fade present visually

A 45 year old male is anaesthetized for a 4 hour long elective Neurosurgical procedure. After induction with 1mg/kg of rocuronium, it is discovered that the patient has not stopped their clopidogrel as originally planned, and the surgery is cancelled. What would be the best clinical course to follow:

a) ventilated the patient for at least 2 hours and assess for first movements  
b) Use the TOF count after an hour and ventilate the patient in ICU or recovery if no change.  
c) Use sugammadex at a dose of 1mg/kg  
d) Use the PTC to establish when the first switch will appear, and a TOFC to establish the dose of sugammadex that will be effective.

The properties of an ideal nerve stimulator would ideally be:

a) A Monophasic and rectangular waveforms, that is constant current, of adequate chronaxy, and which work with batteries.  
b) A multi waveform, constant current, short duration machine which is built into the anaesthetic machine, with electrodes over the radial nerve.  
c) A constant voltage, long duration waveform of greater than 80 mA, with electrodes over the Temporalis muscle.  
d) A constant current, greater than 80 mA, providing supramaximal stimulus until contraction occurs.

References and further reading:

1. Anaesthesia Monitoring Techniques, Anaesthesia and Analgesia 2002, Hughes, Griffiths  
5. Residual Neuromuscular Blockade , Moi , 2013 . WFSA  
7. Murphy, GS et al. Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: A randomized controlled trial of the effect on neuromuscular and clinical recovery. Anesthesiology 2018; 128:27–37