Pharm-11B8 Describe the terms train-of-four stimulation and double burst stimulation with respect to the peripheral nerve stimulator. Describe their advantages and disadvantages when used to evaluate non-depolarising neuromuscular blockade.

**Background**

Non-depolarising neuromuscular blockers exert muscle relaxation by acting as competitive antagonists of nicotinic acetylcholine receptors at the neuromuscular junction.

The depth of neuromuscular blockade can be assessed using a peripheral nerve stimulator. Train-of-four and double burst are two commonly used modes of stimulation.

**Train-of-Four (TOF) Stimulation**

4 x 0.1 msec stimuli delivered at 2 Hz with a preset current (e.g. 60 ~ 80 mA) sufficient to trigger nerve action potential

Useful measurable parameters include:
- number of twitches observed with TOF stimulation
- TOF ratio: the intensity of the fourth twitch (T₄) compared to the first twitch (T₁)

Designed to assess deep neuromuscular blockade

Correlation with neuromuscular physiology:
Non-depolarising NMBs demonstrate fade such that twitch height of T₄ < T₃ < T₂ < T₁
- T₄ disappears → 70% nAChR receptors blocked
- T₃ disappears → 80% nAChR receptors blocked
- T₂ disappears → 90% nAChR receptors blocked
- T₁ disappears → ≈ 100% nAChR receptors blocked
- TOF T₄:T₁ ratio > 0.9 → adequate for extubation

**Double Burst Stimulation (DBS)**

3 x 0.2 msec stimuli at 50 Hz → 0.75 sec pause → 3 x 0.2 msec stimuli at 50 Hz stimuli at preset current (usu. 60 ~ 80 mA) sufficient to trigger nerve action potential

Measured parameter = visual assessment of twitch height of second burst relative to first burst → allows more sensitive measure of fade

Designed to detect even small degree of fade associated with shallow neuromuscular block

**Reversibility**

TOF count 0 ~ 1 → delay reversal
TOF count ≥ 2 give classical reversal
Advantages and Disadvantages

<table>
<thead>
<tr>
<th>Properties</th>
<th>TOF</th>
<th>DBS</th>
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<tbody>
<tr>
<td>Ease of use</td>
<td>Adv: easy – only need nerve stim</td>
<td>Adv: easy – only need nerve stim</td>
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<tr>
<td>Accuracy – qualitative</td>
<td>Adv: for deep blocks, TOF number is relatively easy to assess</td>
<td>Adv: able to more easily detect subtle fade qualitatively when compared with TOF</td>
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<td>Disadv: for shallow blocks, TOF ratio is very difficult to assess</td>
<td>Disadv: difficult to qualitatively assess deep block</td>
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<td>Studies have shown that fade may be detected qualitatively up to TOF ratio of 0.4</td>
<td>Studies have shown that fade may be detected qualitatively up to TOF ratio of 0.6</td>
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<tr>
<td>Accuracy – quantitative</td>
<td>Adv: can accurately assess shallow blocks using TOF ratio with EMG, accelerometer or kinemyography</td>
<td>Disadv: no more accurate than TOF when used with accelerometer</td>
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<tr>
<td>Discomfort in awake patients</td>
<td>Adv: repeated single twitches → less painful</td>
<td>Disadv: bursts of tetany → more painful</td>
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Examiner’s comments - 67.4% of candidates passed this question.

Train of Four is delivered by 4 identical supramaximal stimuli at about 20 – 50 milliamps, each of .1 sec duration, at 2Hz (2 per second); the sequence may be repeated every 10 – 20 seconds if used ‘continuously’. A synopsis of the twitch height and receptor blockade along with a description of the ratios was well described. Interpretation of depth of blockade based on TOF count/ratio was also well discussed. Confusion about millivolts and milliamps often cropped up.

Double Burst Stimulation described as 2 bursts of 3 tetanic stimulations (.2 msecs duration each) 20 msecs apart at 50 Hz bursts separated by 750 msecs pause. The repeatability takes into account the ‘fatigue’ of the junctions following tetanic stimuli. Discussion of advantaged vs. disadvantages including such topics such as ease of use, accuracy to manual / visual assessment, need for extra objective measurement with eg accelomyography, painful or not, able for awake patients, painful or not, use for depth of block, use for assessing presence of residual blockade, use in reversibility of blockade, need or value of a baseline measurement form a choice of headings to make a comment on. Most candidates were able to mention a few to demonstrate the physical/pharmacological/clinical rationale for the choice of technique used.

Detailed descriptions of where and how to place electrodes, comparison of depolarising and non-depolarising blocks were not part of the question.