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- Bernadette Henrichs, PhD, CRNA, CCRN
  - Merck: Speakers bureau
  - Fresenius Kabi USA, LLC: Advisory board
- S. Krishna Ramachandran, M.D.
  - Fresenius Kabi USA, LLC: Advisory board
- Rachel C. Wolfe, Pharm.D., BCCCP
  - Fresenius Kabi USA, LLC: Advisory board
Learning Objectives

At the conclusion of this activity, participants should be able to

• Discuss the rationale for relevant depth of neuromuscular blockade needed to achieve ideal surgical operating conditions
• Explain approaches for reviewing medications for reversal of neuromuscular blockade that take into account patient safety, clinical outcomes, and pharmacoeconomics
• Address challenges faced by the interprofessional team in influencing changes that improve perioperative medication safety and outcomes related to residual paralysis

Achieving the Appropriate Depth of Neuromuscular Blockade

Bernadette Henrichs, Ph.D., CRNA, CCRN
Goldfarb School of Nursing at Barnes-Jewish College
Department of Anesthesiology, Washington University in St. Louis
St. Louis, Missouri
Muscle Relaxation Often Needed During Surgery

• Serves as a major component of providing anesthesia in many surgical cases
  – Analgesia, Amnesia, Muscle Relaxation
• Does not produce unconsciousness, analgesia or amnesia
  – Should never be given without sedation medication
• Prevents patient from moving while surgeon operates
• Relaxes muscle, making operating conditions ideal for surgeon to operate

Muscle Relaxation

• May occur from regional nerve block or neuromuscular blocking agents (muscle relaxants)
• May be potentiated by inhalational agents in a dose-related manner or by certain medications, such as magnesium or aminoglycosides (e.g., gentamicin)
• Can be antagonized by calcium and by anticholinesterases (reversal agents)

Muscle Relaxation

• Neuromuscular blocking agents have varying effects on different muscles
  – Diaphragm is less susceptible to the effects compared with both peripheral muscles and pharyngeal upper airway dilator muscles
  – Diaphragmatic function returns more rapidly than peripheral muscles


Muscle Relaxants

• Risk of residual neuromuscular blockade (NMB) is one of the most feared complications of anesthesia
• Intermediate-acting neuromuscular blockers (e.g., rocuronium, vecuronium, atracurium) have an incidence of residual NMB of over 20%, even after short surgical procedures
• Residual NMB may also occur after a single intubating dose of intermediate-acting neuromuscular blockers
• Quantitative monitoring is presently considered the only recommended method to diagnose residual NMB

To Paralyze or Not Paralyze

• Some anesthesia providers think muscle relaxants should always be administered as part of the anesthetic regimen to ensure patient safety (unless contraindicated due to EMG or motor monitoring)
• Other anesthesia providers advocate for not administering a muscle relaxant as part of the anesthetic regimen

EMG = electromyography

Muscle Relaxation with Anesthetic Induction

• Reverses muscle rigidity that may occur from opioids given with induction
• Eases ventilation after induction of anesthesia
• Allows the vocal cords to relax and open for placement of the endotracheal tube into the trachea without injury to the vocal cords
• Prevents laryngospasm during intubation
• Prevents patient from clenching teeth or moving during intubation

Muscle Relaxation During Surgery

- Allows muscles of abdomen to be relaxed for surgeon
- Deep NMB provides better operating conditions for a variety of surgeries compared with moderate, shallow, or no NMB
- Prevents coughing and movement during certain surgeries
- Allows relaxation of hip joint for laparoscopic hip surgery


Muscle Relaxation for Abdominal Surgery

- Provides adequate surgical operating conditions
- Eliminates abdominal muscle tone
  - Allows surgical exposure and closure with ease
- Prevents spontaneous breathing and diaphragmatic movement during surgery
- May decrease incisional herniation
- May decrease bleeding
- May decrease morbidity and mortality

**Muscle Relaxation for Laparoscopic Surgery**

- Increasing evidence suggests that “only deep NMB may achieve best operating conditions during laparoscopic surgery”
- Deep muscle relaxation superior vs. surgeon increasing intraabdominal pressure
- Allows intraabdominal pressure to be lower (8-10 mm Hg vs. 10-15 mm Hg), which can lead to
  - Significantly reduced postoperative pain
  - Improved patient outcomes and improved quality of life ratings
  - Earlier hospital discharge
  - Less impaired organ perfusion and organ dysfunction (renal, hepatic, cardiac) from macrovascular or microvascular changes that may occur with higher pressures


**Muscle Relaxation for Cardiac Surgery**

- Facilitates tracheal intubation
- Decreases oxygen consumption during cardiopulmonary bypass by up to 30%
- Prevents movement during cannulation
- Attenuates shivering
- Decreases skeletal muscle contraction with defibrillation

Contrera MA et al. Anesthesia for cardiac surgery.
Paralyzing the Patient for Surgery

**Advantages**
- Better operating conditions for surgeon due to muscle relaxation
- Patient will not move or cough despite surgical stimulation
- Lighter anesthetic can be given without risk of patient movement
- Emergence from anesthesia will be quicker

**Disadvantages**
- Muscle relaxants have no anesthetic or hypnotic effects (risk of awareness)
- Increased complications: histamine release, anaphylaxis, myalgia with succinylcholine, residual NMB with nondepolarizing agents
- Increased HR and BP may occur with sympathetic stimulation and lighter anesthesia
- Reversal agents needed if any depth of NMB is present at end of surgery

HR = heart rate  
BP = blood pressure


---

Adverse Effects of Anticholinesterase Inhibitors: Neostigmine

- Confusion
- Bronchoconstriction
- Abdominal cramping, nausea, vomiting
- Parasympathetic stimulation: bradycardia, asystole
- Muscle weakness
- Increased intestinal tone
- Loss of bowel or bladder control
- Excessive salivation

Not Paralyzing the Patient for Surgery

**Advantages**
- Decreases anesthetic awareness
  - If patient moves, anesthesia provider will deepen anesthetic, preventing recall
- No need for reversal agents
- Prevents residual NMB

**Disadvantages**
- Deeper anesthetic needed to prevent movement
- If patient coughs, may lead to injury
  - Head in pins → lacerations at pin site; injury to neck
  - Trocar inserted for laparoscopic surgery → accidental injury to major vessel
- Prolongs emergence - deeper anesthetic
- Patient may need vasopressor support


---

If patient is paralyzed, what depth of NMB is needed?

<table>
<thead>
<tr>
<th>Depth of Block</th>
<th>Quantitative Measurement</th>
<th>Qualitative Measurement</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete block</td>
<td>PTC = 0</td>
<td>PTC = 0</td>
<td>Head in pins; laparoscopic abdominal or hip surgery</td>
</tr>
<tr>
<td>Deep block</td>
<td>PTC ≥ 1; TOF = 0</td>
<td>PTC ≥ 1; TOF = 0</td>
<td>No breathing or diaphragmatic movement</td>
</tr>
<tr>
<td>Moderate block</td>
<td>TOF = 1-3</td>
<td>TOF = 1-3</td>
<td>Many surgeries where deep block not needed</td>
</tr>
<tr>
<td>Shallow block</td>
<td>TOF ratio &lt; 0.4</td>
<td>TOF = 4; fade present</td>
<td>Muscle relaxant not necessarily needed</td>
</tr>
<tr>
<td>Minimal block</td>
<td>TOF ratio = 0.4-0.9</td>
<td>TOF = 4; fade not detected</td>
<td>Not yet ready for extubation</td>
</tr>
<tr>
<td>Acceptable recovery</td>
<td>TOF ratio ≥ 0.9</td>
<td>Cannot be determined</td>
<td>Ready for extubation</td>
</tr>
</tbody>
</table>

PTC = post-tetanic count, TOF = train-of-four

Depth of Neuromuscular Blockade

• Anesthesia providers and surgeons must work together to agree on an acceptable depth of NMB to ensure patient safety

• If muscle relaxation is needed, paralysis should be reversed to decrease the risk of residual NMB

Key Takeaways

• Muscle relaxation may provide ideal operating conditions for the surgeon

• However, this may not always be the safest method in providing anesthesia to the patient

• Surgeons and anesthesia providers must work together to ensure that the anesthetic given is what is best for the patient
Approaches for Reviewing Medications for Reversal of Neuromuscular Blockade

Rachel C. Wolfe, Pharm.D., BCCCP
Perioperative Services and Surgical Critical Care
Barnes-Jewish Hospital
St. Louis, Missouri

Neostigmine
- Acetylcholinesterase (AChE) inhibitor
  - Prevents breakdown of acetylcholine (ACh)
  - Increased competition at the nicotinic receptor

Sugammadex
- Selective relaxant binding agent
- Forms a complex with selected aminosteroid NMBAs
  - Sugammadex affinity
    - Rocuronium > vecuronium
    - No affinity for other NMBAs

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Key Attributes of the Reversal Agents

**Neostigmine**
- Competitive mechanism of action that has the ability to reverse all NMBAs
- Ineffective for reversing profound or deep neuromuscular block
- May reverse moderate block, but takes a significant amount of time
- Effectively reverses minimal to light block within 10-15 minutes in most patients
- Anticholinergic (e.g., glycopyrrolate) coadministration required to prevent bradycardia
- Adverse effects, such as PONV and bradycardia, are more prevalent than with sugammadex
- Residual NMB (defined as a TOF ratio < 0.9) is more prevalent than with sugammadex

**Sugammadex**
- Predictable, highly effective reversal agent for rocuronium and vecuronium only
- Effectively reverses shallow to deep, and even profound block
- Emergent reversal (~3 min from induction) is only approved for rocuronium-induced blockade
- Associated with hypersensitivity reactions (mechanism unknown, unlikely IgG- or IgE-mediated)
- Drug cost is higher than the combination of neostigmine + glycopyrrolate

PONV = postoperative nausea and vomiting


Pharmacoeconomic Considerations

- Medication efficacy
- Medication safety
- Medication cost
- Medication use
- Adjunctive medications
- OR time and OR cost
- OR efficiency
- NMB monitoring: equipment availability, use practices, and cost
- Patient safety: ADE, emergent reversal option
- Residual NMB: reintubation, ICU admission, PACU respiratory event
- PONV incidence
- Readiness for discharge
- PACU time and PACU cost
- Patient education

PACU = post anesthesia care unit; ADE = adverse drug event

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Shift in the Healthcare Mindset

- Agency for Healthcare Research and Quality (AHRQ)
  - U.S. Department of Health and Human Services
  - Value-based care is a core healthcare priority
  - Goal: 20% reduction in hospital-acquired conditions (HACs) between 2014-2019
  - Category: All other HACs
    - Postoperative respiratory failure
    - Postoperative pneumonia
- Potential strategies to reduce postoperative HACs
  - Optimize use of NMM and NMB reversal agents

NMM = neuromuscular monitoring


Quality and Value-Based Healthcare

- Budgetary silos
  - Have the potential to constrain medication use
  - No direct return on investment
- All are tasked to improve health outcomes, reduce unnecessary use, and control healthcare expenditures
**Interprofessional Approach**

- Clinical tactics to NMM and NMB reversal are strategically evaluated to optimize return on investment (ROI)

\[
\text{ROI} = \frac{\text{Net return from reduced postoperative HACs}}{\text{Investment in optimal management of NMB}}
\]


**Pharmacy Department Investment**

- **Drug cost**
  - NMB Reversal - Shallow
    - Neostigmine plus glycopyrrolate $30-65
    - Sugammadex $90
  - NMB Reversal - Moderate
    - Neostigmine plus glycopyrrolate $30-130
    - Sugammadex $90-165
  - NMB Reversal - Deep†
    - Sugammadex $165
  - NMB Reversal - Emergent†
    - Sugammadex $495

*Based on average health-system purchase price of a single-dose or single-use vial or prefilled syringe & weight of 85 kg.
†Neostigmine is ineffective for reversing profound or deep neuromuscular block.
Perioperative and Anesthesiology Investment

**Investment**

- Neuromuscular monitoring equipment (quantitative preferred)
  - Availability and accessibility of user-friendly devices
  - Device acquisition costs ($800-2400 per device)
- Equipment training and competency maintenance
  - Difference in clinical, subjective, and objective monitoring
  - Appropriate electrode placement sites
  - Pre-planning with quantitative monitors (e.g., placement and calibration before NMBA)
  - NMM required for sugammadex as well as neostigmine
- Institutional practice guideline on clinical management and monitoring of NMB


Workflow Efficiency

**Return on Investment**

- Meta-analysis: sugammadex vs. neostigmine
  - Operating room recovery time
    - Sugammadex faster discharge
      - MD 22.14 min, 95% CI (14.62-29.67), p<0.00001
      - Inclusion of patients with deep block: MD 30.05 min, 95% CI (11.11-48.99), p<0.002
    - PACU length of stay
      - Sugammadex faster discharge
        - MD 16.95 min, 95% CI (0.23-33.67), p=0.0469

- Impact on intraoperative & PACU efficiency
  - Reduction in staffing costs
  - Reduction in overtime pay
  - Enhanced employee satisfaction
  - Enhanced patient satisfaction
- Key considerations
  - Discharge vs. discharge-readiness
  - Clinical significance of time saved
    - Enough time saved for an additional case
    - Avoidance of placing OR on hold and case cancellation


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Clinical Outcomes

Potential Return on Investment

- Reduced mechanical ventilation in PACU
- Reduced respiratory events in PACU
- Reduced postoperative pulmonary complications
- Decreased unplanned ICU admissions
- Faster recovery of bowel function
- Decreased readmissions


RECITE Study:
Incidence of Postoperative Residual NMB

NMB at Extubation

- Only 36% had TOF ratio ≥ 0.9
- 73.9% reversed with Neostigmine

NMB on Arrival to PACU

- Only 43% had TOF ratio ≥ 0.9
- 72% reversed with Neostigmine

Incidence Postoperative Residual NMB

![Graph showing TOF ratio within 5 minutes of PACU Admission]

TOF ratio within 5 minutes of PACU Admission

- **Sugammadex (n=74)**
  - TOF ≥0.9: 100%
  - TOF ≥ 0.8 to <0.9: 57%
  - TOF ≥0.7 to <0.8: 21%
  - TOF ≥0.6 to < 0.7: 12%
  - TOF <0.6: 4%
- **Neostigmine + glycopyrrolate (n=76)**
  - TOF ≥0.9: 0%
  - TOF ≥ 0.8 to <0.9: 0%
  - TOF ≥0.7 to <0.8: 0%
  - TOF ≥0.6 to < 0.7: 4%
  - TOF <0.6: 7%


Residual NMB and PACU Respiratory Events

- Incidence of critical respiratory events (CRE) within 15 min of PACU admission was 0.8% (61/7459)
  - Reintubation rate of 0.1% (8/7459)
    - Similar to previous estimates of 0.1-0.2%
- 42/61 patients were matched with controls
  - Criteria: age, sex, procedure
  - Significant residual NMB in cases with CRE vs. controls
    - TOF ratio 0.62 ± 0.2 vs. TOF ratio 0.98 ± 0.07, p<0.0001
    - Severe residual NMB (TOF ratio < 0.7) was present in 73.8% of cases with CRE vs. 0% in the control group

### Postoperative Pulmonary Complications

<table>
<thead>
<tr>
<th>Author &amp; Journal</th>
<th>Study Design Intervention</th>
<th>Primary Outcome</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grosse-Sundrup M. BMJ. 2012; 345:e6329</td>
<td>Prospective PMC N=18,579 (matched)</td>
<td>Receipt of intermediate-acting NMBA</td>
<td>Desaturation after extubation (O₂ Sat &lt; 90% and with decrease in O₂ Sat after extubation) and reintubation within 7 days</td>
</tr>
<tr>
<td>Bulka CM. Anesthesiology 2016; 125:647-55</td>
<td>Retrospective PMC N=1,455 NMBA vs. No NMBA N=1,320 Neostigmine vs. No reversal</td>
<td>Receipt of intermediate-acting NMBA</td>
<td>Incidence of pneumonia within 30 days after surgery</td>
</tr>
</tbody>
</table>

PMC = Propensity matched cohort, OR = odds ratio, CI = confidence interval

### Postoperative Pulmonary Complications

<table>
<thead>
<tr>
<th>Design</th>
<th>Intervention</th>
<th>Primary Outcome</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicenter, prospective, observational European cohort study 211 hospitals</td>
<td>Observational study of patients receiving general anesthesia for non-cardiac surgery</td>
<td>Incidence of postoperative pulmonary complications (PPC) at 28 days</td>
<td>• PPC incidence: 7.6% (1,658/21,694) • PPC incidence with NMBA: 8.4% (1,441/17,150) • Increased risk with NMBA (ARRadj -4.4, 95% CI -5.5 to -3.2)</td>
</tr>
</tbody>
</table>

**Major risk factors for PPC**
- Intrathoracic or open upper abdominal surgery
- Surgery duration > 2 hr
- Preoperative SpO₂ of ≤ 94%
- Emergent surgery
- ASA class ≥ 3
- Age > 60 yr

**Subgroup analysis (selective NMM and reversal agent use)**
- NMBA increased incidence of PPC (ORadj 1.86, 95% CI 1.53-2.26)
- NMM did not decrease risk of PPC (ORadj 1.31, 95% CI 1.15-1.49)
- Reversal agents did not decrease risk of PPC (ORadj 1.23, 95% CI 1.07-1.41)

ARRadj = adjusted absolute risk reduction; ASA = American Society of Anesthesiologists; ORadj = adjusted odds ratio

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Optimizing ROI

- Postoperative pulmonary complications
  - Increase patient morbidity and mortality
  - Increase healthcare expenditures
  - Relatively common
- Preventative measures could be a significant source of cost savings
  - Optimal clinical management of NMB
- Identify patients at high risk for pulmonary complications
  - Enhance return on investment


Risk Prediction Models

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## Risk Stratification

### Patients at High Risk for Postoperative Pulmonary Complications

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative SpO₂ ≤ 94%</td>
<td></td>
</tr>
<tr>
<td>ASA class ≥ 3</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 60 yr</td>
<td></td>
</tr>
<tr>
<td>Duration of procedure &gt; 2 hr</td>
<td></td>
</tr>
<tr>
<td>Intrathoracic or upper abdominal surgery</td>
<td></td>
</tr>
<tr>
<td>Long-acting NMBA</td>
<td></td>
</tr>
<tr>
<td>Severe respiratory disease</td>
<td></td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td></td>
</tr>
<tr>
<td>BMI &gt; 40 kg/m²</td>
<td></td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td></td>
</tr>
<tr>
<td>Significant cardiovascular disease</td>
<td></td>
</tr>
<tr>
<td>History of recent respiratory infection</td>
<td></td>
</tr>
</tbody>
</table>


## Reviewing Reversal Agents

- Interprofessional collaboration
- Multidepartment investment
- Value-based healthcare focus
- Strategy to optimize ROI
- Leadership support
- Continued focus on clinical outcomes
- Understanding of clinical practice
Understanding Clinical Practice

- Utilization
  - % of patients with general anesthesia
  - % of patients receiving NMBAs
  - % using neostigmine
  - % using sugammadex
- Dosage and vial size
  - Appropriate for patient’s weight
  - Appropriate for depth of blockade
  - Appropriate for renal function
- NMM
  - Qualitative vs. quantitative
  - TOF or TOF ratio prior to extubation
  - Competency
- Accessibility impact
  - Stored in ADC, Rx satellite
- Neostigmine with sugammadex rescue
  - Failed reversal with neostigmine ($$$)
  - Neostigmine-related neuromuscular weakness
- Sugammadex 16 mg/kg use for emergent reversal
- Postoperative clinical outcomes
  - PACU respiratory events
  - Reintubation rates
  - Unplanned ICU admissions
  - Postoperative pulmonary complications
  - Complications from use of anticholinergic agents
  - Hypersensitivity reactions

Key Takeaways

- Pharmacy review of NMB reversal agents must consider impact beyond the pharmacy budget
- Interprofessional effort is required to obtain the best return on investment
- Clinical outcome data on sugammadex are limited
- Optimal clinical management of NMB is undefined

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Influencing Change to Improve Perioperative Medication Safety and Outcomes

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Beth Israel Deaconess Medical Center and Harvard Medical School
Boston, Massachusetts

Elements of Implementation Success

- Intervention characteristics
- Outer setting
- Inner setting
- Characteristics of individuals
- Implementation process


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## Intervention Characteristics

<table>
<thead>
<tr>
<th>Intervention Source</th>
<th>Perception of key stakeholders about whether the intervention is externally or internally developed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence Strength &amp; Quality</td>
<td>Stakeholders’ perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes</td>
</tr>
<tr>
<td>Relative Advantage</td>
<td>Stakeholders’ perception of the advantage of implementing the intervention versus an alternative solution</td>
</tr>
<tr>
<td>Adaptability</td>
<td>Degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs</td>
</tr>
</tbody>
</table>

| Trialability                  | Ability to test the intervention on a small scale in the organization and ability to reverse course (undo implementation) if warranted |
| Complexity                   | Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement |
| Design Quality and Packaging | Perceived excellence in how the intervention is bundled, presented, and assembled |
| Cost                         | Costs of the intervention and costs associated with implementing that intervention, including investment, supply, and opportunity costs |

<table>
<thead>
<tr>
<th>Patient Needs &amp; Resources</th>
<th>Extent to which patient needs, as well as barriers and facilitators to meet those needs, are accurately known and prioritized by the organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosmopolitanism</td>
<td>Degree to which an organization is networked with other external organizations</td>
</tr>
<tr>
<td>Peer Pressure</td>
<td>Mimetic or competitive pressure to implement an intervention; typically because most or other key peer or competing organizations have already implemented or are in a bid for a competitive edge</td>
</tr>
</tbody>
</table>


| External Policy & Incentives | Broad construct that includes external strategies to spread interventions, including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaborations, and public or benchmark reporting |


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### Inner Setting

<table>
<thead>
<tr>
<th>Structural Characteristics</th>
<th>Social architecture, age, maturity, and size of an organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Networks &amp; Communications</td>
<td>The nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organization</td>
</tr>
<tr>
<td>Culture</td>
<td>Norms, values, and basic assumptions of a given organization</td>
</tr>
<tr>
<td>Implementation Climate</td>
<td>Absorptive capacity for change, shared receptivity of involved individuals to an intervention and the extent to which use of that intervention will be rewarded, supported, and expected within the organization</td>
</tr>
<tr>
<td>Readiness for Implementation</td>
<td>Tangible and immediate indicators of organizational commitment to the decision to implement an intervention</td>
</tr>
</tbody>
</table>

Characteristics of Individuals

• Knowledge and beliefs about the intervention
• Self-efficacy
• Individual stage of change
• Individual identification with organization
• Other personal attributes

Implementation Process
Implementation Process

• Planning
• Engaging
  – Opinion leaders
  – Formally appointed internal implementation leaders
  – Champions
  – External change agents
• Executing
• Reflecting and evaluating


Relative Numbers of Constructs


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So What Actually Works?

<table>
<thead>
<tr>
<th>Strong Differentiators</th>
<th>Low Implementation Success</th>
<th>High Implementation Success</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTERVENTION CHARACTERISTICS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative advantage</td>
<td>-2</td>
<td>+1</td>
</tr>
<tr>
<td><strong>OUTER SETTING</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient needs and resources</td>
<td>-2</td>
<td>0 (mixed)</td>
</tr>
<tr>
<td><strong>INNER SETTING</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Networks and communications</td>
<td>-2</td>
<td>-2</td>
</tr>
<tr>
<td>Implementation climate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tension for change</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Relative priority</td>
<td>-1</td>
<td>-2</td>
</tr>
<tr>
<td>Goals and feedback</td>
<td>-2</td>
<td>-1</td>
</tr>
<tr>
<td>Learning climate</td>
<td>Missing</td>
<td>-1</td>
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<tr>
<td>Readiness for implementation</td>
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<td></td>
</tr>
<tr>
<td>Leadership engagement</td>
<td>-2</td>
<td>-1</td>
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<tr>
<td><strong>IMPLEMENTATION PROCESS</strong></td>
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<td></td>
</tr>
<tr>
<td>Planning</td>
<td>-1</td>
<td>Missing</td>
</tr>
<tr>
<td>Reflecting and evaluating</td>
<td>-1</td>
<td>-2</td>
</tr>
</tbody>
</table>

Damschroder et al. *Implementation Science*. 2013, 8:51.
Study Design

- Study start date: Jan 2014
- Reduction in aliquot size
- QI bonus stops: Dec 2015
- Study ends

Pre-intervention period

Distribution of cognitive aid
Educational activities
QI bonus starts

QI = quality improvement


Neostigmine Reversal Guide

<table>
<thead>
<tr>
<th>Type of Monitoring</th>
<th>Neostigmine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualitative</td>
<td>Weight-Based</td>
</tr>
<tr>
<td>No twitch</td>
<td>WAIT</td>
</tr>
<tr>
<td>1 twitch</td>
<td>WAIT</td>
</tr>
<tr>
<td>2-3 twitches</td>
<td>~50 mcg/kg</td>
</tr>
<tr>
<td>4 twitches with fade</td>
<td>~40 mcg/kg</td>
</tr>
<tr>
<td>4 twitches without fade</td>
<td>15-30 mcg/kg</td>
</tr>
<tr>
<td>TOF ratio &gt;0.9</td>
<td>NONE</td>
</tr>
</tbody>
</table>

Risk factors for Residual Weakness

- High total dose of NMBA >1.5 mcg/kg rocuronium or >0.4 mg/kg cisatracurium
- High dose neostigmine reversal >60 mcg/kg

ALWAYS DOSE NMBA AND REVERSAL ACCORDING TO MONITORING AND CLINICAL CONDITION

Mean Neostigmine Dose


Excessive Neostigmine Dose (>60 mcg/kg)


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Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre-QI Intervention n= 2,937</th>
<th>Post-QI Intervention n=9,088</th>
<th>Adjusted OR (95% CI)</th>
<th>IRR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRC(^a)</td>
<td>220 (7.5%)</td>
<td>568 (6.3%)</td>
<td>0.73 (0.61-0.88)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital LOS(^b)</td>
<td>5.3 ± 7.5</td>
<td>5.0 ± 7.2</td>
<td>0.91 (0.87-0.94)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Costs ($)(^b) Median [IQR]</td>
<td>14943 [9121, 24836]</td>
<td>14493 [8804, 24017]</td>
<td>0.95 (0.93-0.97)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\)Odds ratio, derived from logistic regression.  
\(^b\)Incidence rate ratio, derived from zero-truncated negative binomial regression.

IRR = incidence rate ratio, IQR = interquartile range,  
PRC = postoperative respiratory complications, LOS = length of stay

Why was this intervention successful?

Evidence for Dosing and Monitoring

- Use of NMBA independently associated with PRC
- Higher doses of intermediate-acting NMBA associated with dose-dependent increases in incidence of PRC
- Appropriate reversal may limit risk of PRC associated with high dose NMBA
- Use of quantitative monitoring may be associated with lower risk of PRC


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Appropriate Reversal Can Be a QI Target

<table>
<thead>
<tr>
<th>NMBA Dose Quintiles (x ED95 dose)</th>
<th>Appropriate Reversal</th>
<th>Inappropriate Reversal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PRC rate</td>
<td>Effect Size</td>
</tr>
<tr>
<td>I (Lowest)</td>
<td>0.39%</td>
<td>n/a</td>
</tr>
<tr>
<td>II</td>
<td>0.45%</td>
<td>1.04 (0.7-1.6)</td>
</tr>
<tr>
<td>III</td>
<td>0.60%</td>
<td>1.16 (0.8-1.7)</td>
</tr>
<tr>
<td>IV</td>
<td>0.63%</td>
<td>0.95 (0.6-1.4)</td>
</tr>
<tr>
<td>V (Highest)</td>
<td>0.91%</td>
<td>0.98 (0.6-1.5)</td>
</tr>
</tbody>
</table>

Appropriate reversal (neostigmine ≤0.06 mg/kg at TOF count of at least 2)
Inappropriate reversal (no neostigmine administration, neostigmine administration not guided by TOF count or doses >0.06 mg/kg)

ED95 = effective dose to produce 95% depression in twitch height


Key Takeaways

• Process modification through change management in the OR is complex
  – Art of anesthesia
• Implementation science constructs are valid
  – Reflect on how past interventions succeeded or failed in your environment
• Residual NMB is largely preventable through effective change management

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Selected Resources


Strategies for the Interprofessional Team: Faculty Discussion and Questions

- Providing ventilation support for patients in the PACU who have deep block
- Using quantitative monitoring
- Incorporating cost-effectiveness studies into P&T evaluations
- Providing patient education about interaction of sugammadex and hormonal contraceptives
- Enhancing patient safety after neuromuscular blockade
- Paying attention to definitions (e.g., postoperative respiratory complications) when assessing outcomes

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About the Faculty

Rachel C. Wolfe, Pharm.D., BCCCP, Activity Chair
Clinical Pharmacy Specialist
Perioperative Services and Surgical Critical Care
Barnes-Jewish Hospital
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Rachel C. Wolfe, Pharm.D., BCCCP, is Clinical Pharmacy Specialist of Perioperative Services and Surgical Critical Care at Barnes-Jewish Hospital and Washington University Medical Center in St. Louis, Missouri. She is also Adjunct Clinical Instructor for the Barnes-Jewish Hospital Goldfarb School of Nursing and St. Louis College of Pharmacy.

Dr. Wolfe earned her Doctor of Pharmacy degree from St. Louis College of Pharmacy. She completed her residency training at University of Kentucky HealthCare, and she is board certified in critical care.

At Barnes-Jewish Hospital, Dr. Wolfe is responsible for the provision of clinical pharmacy services in the perioperative and periprocedural environment and for the coordination of clinical services provided by four operating room pharmacy satellites. She also serves as a preceptor for Doctor of Pharmacy students and pharmacy residents and is co-chair of the analgesia subcommittee of the Pharmacy & Therapeutics committee. Dr. Wolfe collaborates closely with the Department of Anesthesiology to develop and implement evidenced-based protocols and plays an integral role in the enhanced surgical recovery initiatives that span across several surgical services. She has led several medication safety and standardization initiatives in addition to initiatives that focus on quality of perioperative care and postoperative patient outcomes.

Dr. Wolfe is a member of the Society of Critical Care Medicine and American College of Clinical Pharmacy. In 2011 she received Barnes-Jewish Hospital’s David A. Gee Meritorious Service Award and Team Award for Quality Improvement for Anesthesia Medication Management.

Bernadette Henrichs, Ph.D., CRNA, CCRN
Director, Nurse Anesthesia Program
Barnes-Jewish College Goldfarb School of Nursing
Director, CRNA Education and Research
Washington University Department of Anesthesiology
St. Louis, Missouri

Bernadette Henrichs, Ph.D., CRNA, CCRN, is Professor and Director of the Nurse Anesthesia Program at the Goldfarb School of Nursing at Barnes-Jewish College in St. Louis, Missouri. She is also Director of CRNA Education and Research in the Department of Anesthesiology at Washington University School of Medicine in St. Louis. In addition, Dr. Henrichs administers anesthesia several days a week.

Dr. Henrichs received her anesthesia training from Washington University School of Medicine, later earning her M.S.N. and Ph.D. degrees from St. Louis University in St. Louis, Missouri.

Dr. Henrichs is an active member of the Missouri Association of Nurse Anesthetists (MoANA), American Association of Nurse Anesthetists (AANA), American Association of Critical-Care Nurses (AACN), Sigma Theta Tau International Honor Society of Nursing, and Society for Simulation in Healthcare. She served on the AANA Board of Directors as Region 4 Director and on the AANA Foundation Board of Trustees.

In addition to authoring several articles and book chapters on anesthesia-related topics, Dr. Henrichs co-edited A Resource for Nurse Anesthesia Educators, 2nd ed. She served on the editorial board and is a reviewer for AANA Journal. In 2017, Dr. Henrichs received the AANA Program Director of the Year Award. She also received the Beverly Krause Outstanding CRNA Clinical Instructor Award in 2014, an honor bestowed by graduates.

S. Krishna Ramachandran, M.D.
Associate Professor of Anaesthesia
Harvard Medical School
Vice Chair of Quality, Safety, and Innovation
Beth Israel Deaconess Medical Center
Boston, Massachusetts

S. Krishna Ramachandran, M.D., is Associate Professor of Anaesthesia at Harvard Medical School and Vice Chair of Quality, Safety, and Innovation in the Department of Anesthesiology at Beth Israel Deaconess Medical Center in Boston.

Dr. Ramachandran is a nationally recognized leader in patient safety and perioperative quality. As the Vice-Chair of Anaesthesiology, he has developed several programs, including a unique quality tool that connects clinician medication management behaviors with patient and efficiency outcomes. He also led anesthesia clinical change management and surveillance of safety in response to the shortage of intravenous opioids.

Dr. Ramachandran began his career in anesthesia in Pondicherry, India, and developed it further as a specialist registrar in the Oxford Deanery in England. After a successful decade leading quality and safety initiatives at the University of Michigan, he moved to Harvard and Beth Israel Deaconess Medical Center in 2016. He is a faculty member on the Master of HealthCare Quality and Safety program at Harvard Medical School. In addition, he is a busy clinician, educator, and researcher.

Dr. Ramachandran serves on the editorial board of prestigious journals and has published over 60 peer-reviewed studies in top anesthesiology journals, primarily around perioperative cardiorespiratory outcomes. Most recently he co-authored a study looking at the relationship between reducing neostigmine syringe size to 3 mL from the standard 5-mL vial and perioperative respiratory failure rates.

Accreditation

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1.5 contact hours, application-based
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- Neuromuscular Blockade and Reversal: An Overview of Key Concepts (1.0 hr CE)—available NOW on-demand
- Two e-newsletters (total 0.5 hr CE)—available Spring 2019

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