



School of Continuous
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AN OVERVIEW OF PERIOPERATIVE MEDICINE 2023

FROM OUTPATIENT PREOPERATIVE
ASSESSMENT TO INPATIENT
POSTOPERATIVE CARE

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PHYSIOLOGICAL EFFECTS OF ANESTHESIA

WHAT DOES THE MEDICAL CONSULTANT NEED TO
KNOW ABOUT THE PARALYTIC AGENTS AND THE
PHYSIOLOGIC EFFECTS OF ANESTHESIA?

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

All relevant financial relationships have been mitigated.

LEARNING OBJECTIVES

- Participants will be able to identify common complications associated with neuromuscular blockade
- Participants will be able to describe factors that contribute to residual neuromuscular blockade and how they impact post surgical patient outcomes

ARS QUESTION

Use this WF2491419 for your Audience Response (ARS) portion of your presentation. This format meets the requirements of MOC and AV.

What is the most common postoperative complication associated with neuromuscular blockade agents (NMBA) aka “paralytics?”

1. Anaphylaxis
2. Residual neuromuscular blockade
3. Sedation
4. Postoperative Nausea & Vomiting (PONV)

RATIONALE

Use this WF2491415 for your Audience Response (ARS) portion of your presentation. This format meets the requirements of MOC and AV.

- Between 20-40% of patients arriving in PACU have postoperative residual neuromuscular blockade (PRNB), (Farhan et.al., 2014)
- In study by Belcher et.al., (2017), for patients receiving neuromuscular blockade agent (NMBA) intraoperatively, the incidence of any major complication was 2.1% and for any minor complication was 35.2%.
- PONV and sedation are not associated with PRNB
- Anaphylaxis associated with all NMBA was found to be 29.5 case per million vials (Petitpain et.al. 2018)

REFERENCE(S):

Farhan, H., Moreno-Duarte, I., McLean, D., & Eikermann, M. (2014). Residual Paralysis: Does it Influence Outcome After Ambulatory Surgery?. *Current anesthesiology reports*, 4(4), 290–302. <https://doi.org/10.1007/s40140-014-0073-6>

Belcher, A. W., Leung, S., Cohen, B., Yang, D., Mascha, E. J., Turan, A., Saager, L., & Ruetzler, K. (2017). Incidence of complications in the post-anesthesia care unit and associated healthcare utilization in patients undergoing non-cardiac surgery requiring neuromuscular blockade 2005-2013: A single center study. *Journal of clinical anesthesia*, 43, 33–38. <https://doi.org/10.1016/j.jclinane.2017.09.005>

Petitpain, N., L Argouillon, Kamel Masmoudi, Fedrizzi, S., Cottin, J., C. Latache, Mertes, P.-M., & Gillet, P. (2018). *Neuromuscular blocking agents induced anaphylaxis: Results and trends of a French pharmacovigilance survey from 2000 to 2012*. 73(11), 2224–2233. <https://doi.org/10.1111/all.13456>

ARS QUESTION

Use this WF2491419 for your Audience Response (ARS) portion of your presentation. This format meets the requirements of MOC and AV.

Which is the mechanism that residual neuromuscular blockade contributes to postoperative pulmonary complications?

1. Bronchospasm
2. Hypotension
3. Bradycardia
4. Impairment of normal respiratory physiology

RATIONALE

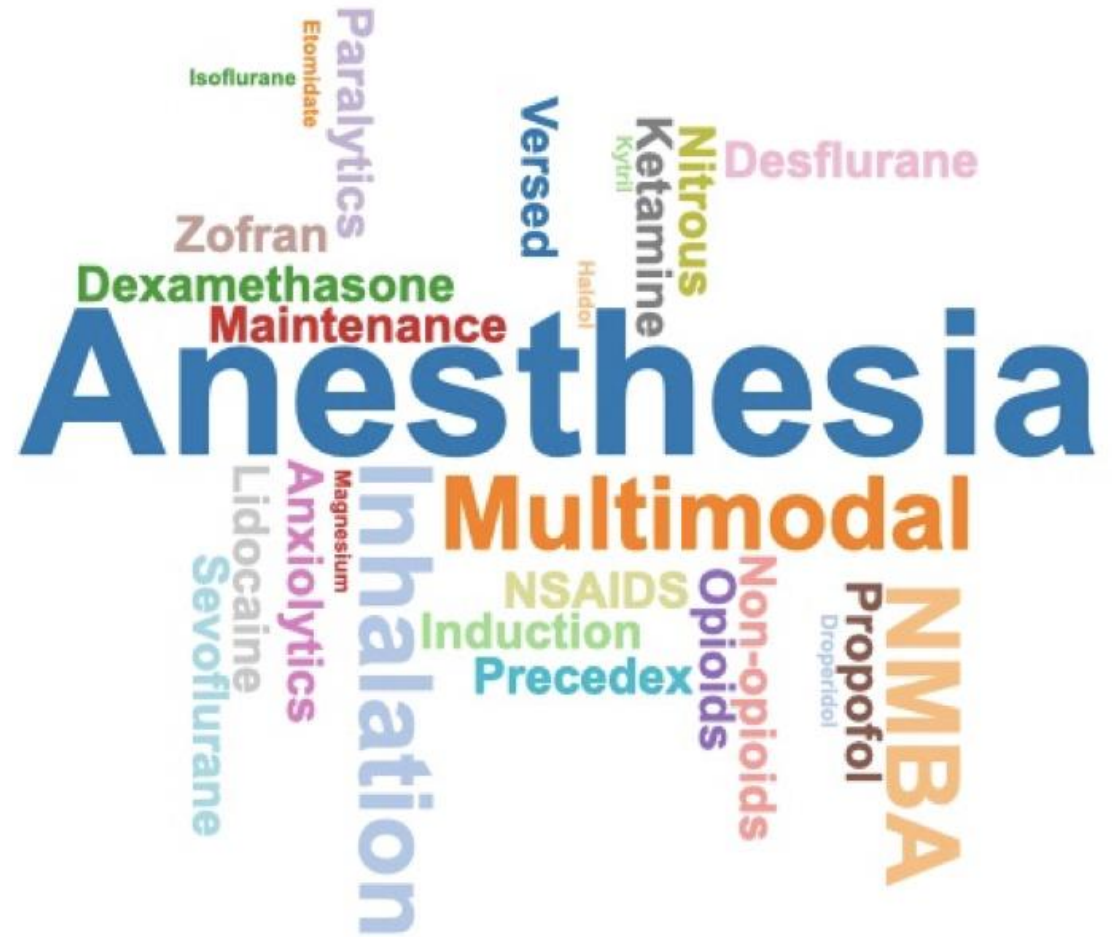
Use this WF2491415 for your Audience Response (ARS) portion of your presentation. This format meets the requirements of MOC and AV.

- Respiratory events are the most common complication of postoperative residual neuromuscular block (PRNB), (Farhan et.al., 2014).
- Respiratory events are due to impairment of normal respiratory physiology including:
 - Impaired respiratory drive (hypoxic ventilatory response)
 - Impaired respiratory muscle function (respiratory pump muscle, upper airway dilator muscle, & abdominal muscle function)
 - Impaired ability to protect the airway during swallowing
- Impairment of normal respiratory physiology leads to atelectasis, upper airway obstruction and impaired cough/ability to clear secretions, increasing risk of respiratory complications.

REFERENCE(S):

Farhan, H., Moreno-Duarte, I., McLean, D., & Eikermann, M. (2014). Residual Paralysis: Does it Influence Outcome After Ambulatory Surgery?. *Current anesthesiology reports*, 4(4), 290–302. <https://doi.org/10.1007/s40140-014-0073-6>

PHYSIOLOGICAL EFFECTS OF ANESTHESIA MEDICATIONS



PHYSIOLOGICAL EFFECTS OF ANESTHESIA MEDICATIONS

FOCUS OF DISCUSSION

- Implications for post-surgical care
- Neuromuscular Blocking Agents (NMBA) aka “paralytics”
- Residual Neuromuscular weakness
- Quality Initiatives

PHYSIOLOGICAL EFFECTS OF ANESTHESIA

WHY IS THIS IMPORTANT TO THE MEDICAL CONSULTANT?

Post operative Respiratory Complications are the second most common postoperative surgical complication and lead to marked increased hospital costs and length of stay

Dimick, J. B., MD, Chen, S. L., MD, Tahere, P. A., MD MBA FACS, Henderson, W. G., PhD, Khuri, S. F., MD FACS, & Campbell Jr, D. A., MD FACS (2004). Hospital Cost Associated with Surgical Complications: A Report from the Private-sector National Surgical Quality Improvement Program. *Journal of American College of Surgeons*, 199(4), 531-537. <https://doi.org/10.1016/j.jamcollsurg.2004.05.276>.

POSTOPERATIVE COMPLICATIONS

IMPACT OF HOSPITAL COST & LENGTH OF STAY

Table 4. Relationship of Postoperative Complications to Unadjusted and Adjusted Total Hospital Costs and Length of Stay in the University of Michigan National Surgical Quality Improvement Program

Complication	Attributable increase with complication*			
	Unadjusted	Adjusted for procedure complexity	Adjusted for complexity and patient characteristics	Adjusted for complexity, patient variables, and other complications
Hospital cost analysis, \$ (95% CI)				
Infectious	8,209 (5,566–10,853)	4,798 (4,110–5,486)	2,207 (1,301–3,113)	1,398 (377–2,418)
Cardiovascular	13,256 (6,720–19,799)	13,330 (11,579–15,082)	7,519 (5,607–9,437)	7,789 (5,260–10,317)
Respiratory	54,430 (51,770–57,091)	44,554 (43,753–45,356)	51,409 (49,868–52,950)	52,466 (50,665–54,268)
Thromboembolic	28,355 (22,580–34,130)	15,727 (14,004–17,450)	18,341 (16,422–20,259)	18,310 (15,893–20,728)
Length of stay analysis, d (95% CI)				
Infectious	4.0 (1.6–7.2)	4.4 (1.8–8.2)	2.6 (0.7–5.2)	2.8 (0.8–5.4)
Cardiovascular	2.8 (–1.5–12)	2.7 (–1.5–12)	–0.5 (–2.9–4.4)	–1.5 (–3.4–2.3)
Respiratory	20 (11–34)	18 (8.9–32)	5.8 (1.7–12)	5.5 (1.5–12)
Thromboembolic	15 (5.2–35)	12 (3.0–31)	4.7 (0–14)	2.8 (0.8–5.4)

*Analysis performed using multivariate linear regression.

Dimick, J. B., MD, Chen, S. L., MD, Tahere, P. A., MD MBA FACS, Henderson, W. G., PhD, Khuri, S. F., MD FACS, & Campbell Jr, D. A., MD FACS (2004). Hospital Cost Associated with Surgical Complications: A Report from the Private-sector National Surgical Quality Improvement Program. *Journal of American College of Surgeons*, 199(4), 531-537. <https://doi.org/10.1016/j.jamcollsurg.2004.05.276>.

PHYSIOLOGICAL EFFECTS OF ANESTHESIA

RESPIRATORY COMPLICATIONS

Surgical and Anesthesia Factors are more predictive of respiratory complications than Patient Factors (as compared to cardiac complications)

Surgical Factors

- Emergency surgery
- Long duration of surgery
- Type of surgery

Anesthesia Factors

- Opioids
- Neuromuscular blocking drugs
- General Anesthesia

Patient Factors

- COPD
- Diabetes
- Obesity
- Non-modifiable risk factors, e.g., advanced age, male sex

Karcz, M., & Papadakos, P. J. (2013). Respiratory complications in the postanesthesia care unit: A review of pathophysiological mechanisms. *Canadian journal of respiratory therapy : CJRT = Revue canadienne de la therapie respiratoire : RCTR*, 49(4), 21–29.

PHYSIOLOGICAL EFFECTS OF ANESTHESIA MEDICATIONS

POST OPERATIVE RESPIRATORY FUNCTION



General Anesthesia & Mechanical Ventilation

Alterations in the control of breathing complex

- Chemoreflexes (hypercapnic & hypoxic)
- Non-chemoreflexes:
 - “wakefulness drive” upper airway tone

Variation of effects dependent on patient physiological state



Opioids & Sedatives

Respiratory depression

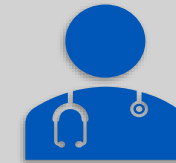
Neuroaxial opioids:

- depress both hypoxic & hypercapnic chemoreflexes
- can be delayed

Midazolam:

- decreases respiratory drive
- reduces hypoxic & hypercapnic chemoreflexes

Synergistic effect



NMBA “paralytics”

Residual neuromuscular blockade: 33% to 64% on arrival to PACU

Post op hypoxia secondary to effects on:

- chemoreceptors
- upper airway patency
- phrenic-nerve diaphragm neuromuscular junction

Karcz, M., & Papadacos, P. J. (2013). Respiratory complications in the postanesthesia care unit: A review of pathophysiological mechanisms. *Canadian journal of respiratory therapy : CJRT = Revue canadienne de la therapie respiratoire : RCTR*, 49(4), 21–29.

PHYSIOLOGICAL EFFECTS OF ANESTHESIA NEUROMUSCULAR BLOCKING AGENTS “PARALYTICS”



Why are neuromuscular blocking agents used?

Facilitate intubation with general anesthesia
Optimize surgical conditions



Commonly used neuromuscular blocking agents used in anesthesia

Depolarizing: Succinylcholine
Non-depolarizing: Rocuronium, Cisatracurium, Vecuronium, (Pancuronium)



Medications used in the reversal of neuromuscular blockade

Neostigmine
Sugammadex

NEUROMUSCULAR BLOCKADE AGENTS (NMBA)

CONSIDERATIONS & CONTRAINDICATIONS

Depolarizing NMBA

e.g., Succinylcholine

- Hyperkalemia
- Bradycardia (pediatrics)
- Increased intracranial and ocular pressure
- Malignant Hyperthermia
- Pseudocholinesterase Deficiency
- Myopathies (e.g., Duchene's muscular dystrophy, elevated CK)

Non-Depolarizing NMBA

e.g., Rocuronium, Vecuronium, Cisatracurium

- Histamine release (bronchospasm, hypotension, vasodilation) with benzoyl
- Renal and Liver disease considerations

Contraindication

Severe allergic reaction or anaphylaxis

NEUROMUSCULAR BLOCKADE REVERSAL MEDICATIONS

- **Neostigmine**

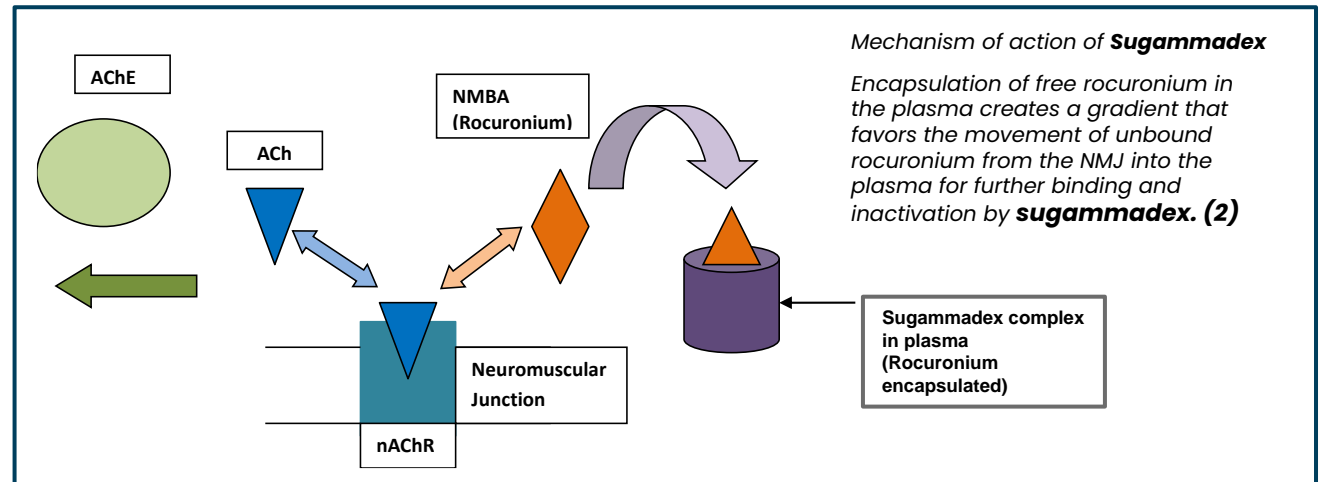
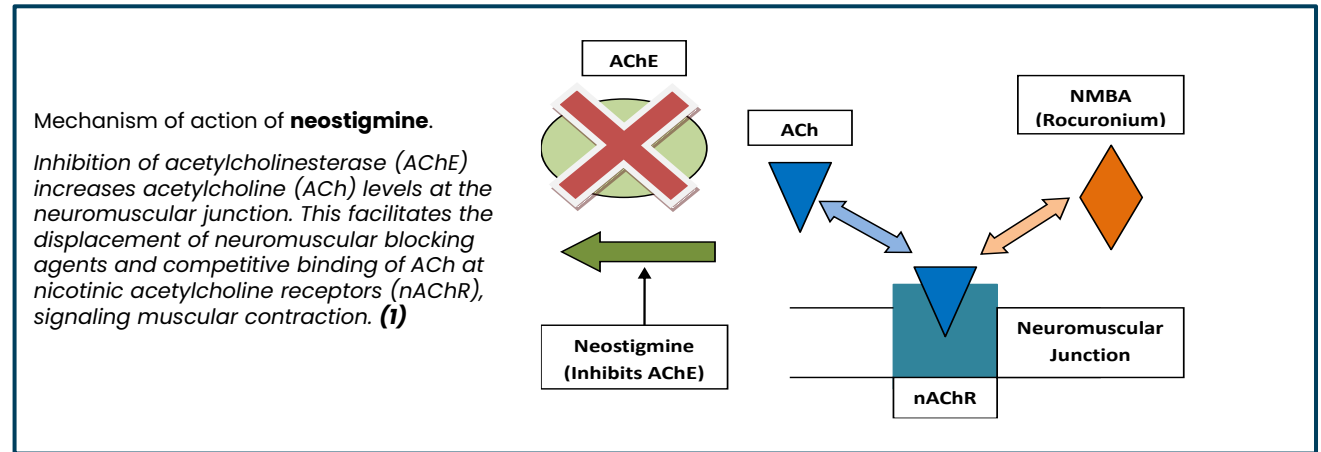
- “ceiling effect”
- Inhibits acetylcholinesterase

- **Sugammadex**

- Encapsulates rocuronium (NMBA)
- Complex renally excreted

- **Monitoring**

- Qualitative vs quantitative
- TOFR >0.9



Residual Neuromuscular Blockade

(1) <https://www.openanesthesia.org/keywords/reversal-of-neuromuscular-blockade-neostigmine/>

(2) <https://www.openanesthesia.org/keywords/reversal-of-neuromuscular-blockade-sugammadex/>

PHYSIOLOGICAL EFFECTS OF ANESTHESIA RESIDUAL NEUROMUSCULAR BLOCKADE

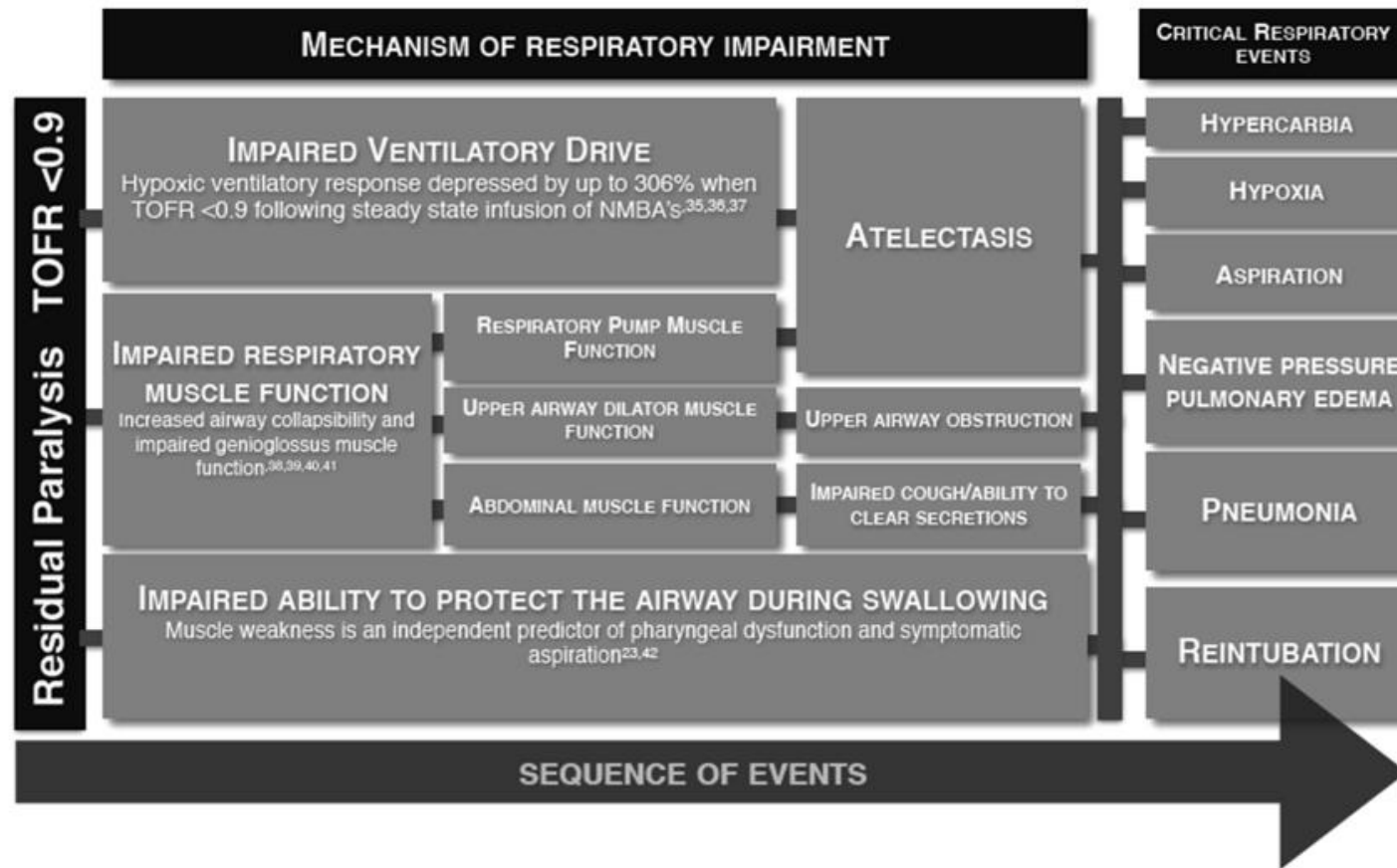


Fig. 1 Mechanisms of residual paralysis induced postoperative respiratory failure. A small level of residual paralysis that cannot be detected without quantitative monitoring of the train-of-four (TOF) response impairs several important facets of respiratory function. The main mechanisms of respiratory failure induced by minimal, residual neuromuscular blockade (TOF: 0.5–0.9) are impairments of hypoxic ventilatory response, and respiratory muscle function. In addition, the coordination between breathing and swallowing is impaired, leading to the inability to protect the airway during swallowing. Consequently, paralysis increases the vulnerability to hypoxia, symptomatic aspiration, pulmonary edema, and reintubation

Farhan, H., Moreno-Duarte, I., McLean, D., & Eikermann, M. (2014). Residual Paralysis: Does it Influence Outcome After Ambulatory Surgery?. *Current anesthesiology reports*, 4(4), 290–302. <https://doi.org/10.1007/s40140-014-0073-6>

RESIDUAL NEUROMUSCULAR BLOCKADE

SPECIAL POPULATIONS



- **Obstructive Sleep Apnea**

- OSA patients may be at higher risk for postoperative hypoxemia, respiratory failure and residual neuromuscular blockade (1)
- Sugammadex may be associated with lower postoperative pulmonary complications compared to Neostigmine (1)

- **Elderly**

- Increased risk of postoperative residual neuromuscular block (PRNB)
- Incidence of PRNB in Elderly 57.7% vs 30% younger patients (99% CI, -41.2 to 13.1%; $p < 0.001$) (2)
- Age related changes in pharmacokinetics & pharmacodynamics (3)
- Renal & Hepatic excretion

(1) Christensson, E., Ebberyd, A., Hårdemark Cedborg, A., Lodenius, Å., Österlund Modalen, Å., Franklin, K.A., Eriksson, L.I. and Jonsson Fagerlund, M. (2020), Hypoxic ventilatory response after rocuronium-induced partial neuromuscular blockade in men with obstructive sleep apnoea. *Anaesthesia*, 75: 338-347. <https://doi.org/10.1111/anae.14806>

(2) Lee, L. A., Athanassoglou, V., & Pandit, J. J. (2016). Neuromuscular blockade in the elderly patient. *Journal of pain research*, 9, 437–444. <https://doi.org/10.2147/JPR.S85183>

(3) Murphy, G. S., Szokol, J. W., Avram, M. J., Greenberg, S. B., Shear, T. D., Vender, J. S., Parikh, K. N., Patel, S. S., & Patel, A. (2015). Residual Neuromuscular Block in the Elderly: Incidence and Clinical Implications. *Anesthesiology*, 123(6), 1322–1336. <https://doi.org/10.1097/ALN.0000000000000865>

Quantitative Neuromuscular Monitoring in Clinical Practice: A Professional Practice Change Initiative

Reducing Residual Neuromuscular Blockade (PRNB) with quantitative monitoring

- Documentation of Train of Four Ratio (TOFR) > 0.9
- Use of Sugammadex
- PACU length of stay/ Ready for discharge decreased
- Hospital length of stay decreased
- Postoperative pulmonary complications (NS; low number of complications)

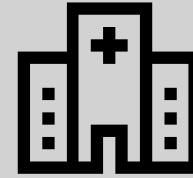
Wade A. Weigel, Barbara L. Williams, Neil A. Hanson, C. Craig Blackmore, Randy L. Johnson, Gary M. Nissen, Andrew B. James, Wyndam M. Strodbeck; Quantitative Neuromuscular Monitoring in Clinical Practice: A Professional Practice Change Initiative. *Anesthesiology* 2022; 136:901–915
doi: <https://doi.org/10.1097/ALN.0000000000004174>

RESIDUAL NEUROMUSCULAR BLOCKADE QUALITY INITIATIVES



PHYSIOLOGICAL EFFECTS OF ANESTHESIA

SUMMARY HIGHLIGHTS



- **Respiratory Complications**
 - Postoperative Residual Neuromuscular Block (PRNB)
- **Considerations for at risk patient groups**
 - OSA & Elderly
- **Quality Initiatives**
 - ASPF/ASA
- **Monitoring**
 - Qualitatively vs Quantitively
- **Pharmacokinetics & Pharmacodynamics**
 - Renal & Hepatic function
- **Reversal Medications**
 - Role of Sugammadex

QUESTIONS & DISCUSSION





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