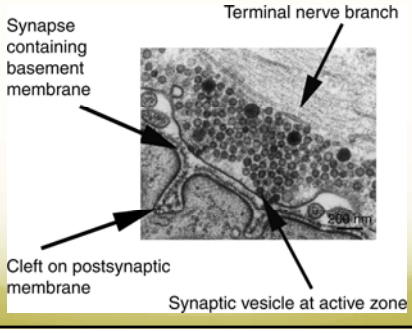
Paralysis in the Surgical Patient: Too Much of a Good Thing.

Tony Oliva, MD/PhD
Assistant Professor
University of Colorado Denver

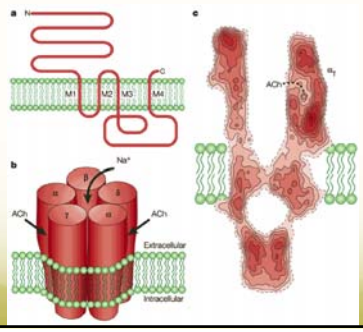
Neuromuscular Junction



Objectives

- Review the historical perspective of neuromuscular blockade
- Review the neuromuscular junction physiology
- Review methods of monitoring neuromuscular function
- Discuss future directions of surgical paralysis and reversal

Acetylcholine Receptor



Pertinent History

- Use of neuromuscular blockers first used in WWII era surgeries
- Shown to be related to increased mortality in 1950's
- In 1970's, residual neuromuscular blockade phrase was coined
- Over 100 million doses of neuromuscular blockers are administered annually in the US

Neuromuscular Blockers

- Succinylcholine
- Benzylisoquinolinium Class
  - Cisatracurium
- Steroid Class
  - Vecuronium
  - Rocuronium

Residual Neuromuscular Blockade (RNMB)

- Is it a problem?
  - Yes
- How do you define the problem?
  - Train of four (TOF) ratio <0.9
- How big of a problem is it?
  - Upward of 40% of patients in PACU are affected
  - Increased risk of airway obstruction, aspiration, hypoxemia, reintubation.

Quantitative Monitors

- Despite being gold standard, it is not often available or used
- Optimal use requires calibration and normalization
- Limitations:
  - Requires a freely moving thumb
  - Is not fail-safe in residual weakness prevention

RNMB continued

- Why is it a problem?
  - Surgeon request for deeper blockade
  - No reversal dose given
  - Inappropriate reversal dose given
  - No use of muscle twitch device
  - Incomplete understanding of how to use and interpret twitch devices
  - Reliance on clinical signs for adequate strength
- What are solutions to the problem?
  - Appropriate neuromuscular function monitoring
  - Appropriate dose of reversal agents

Qualitative Monitor Modes

- TOF
  - Most common mode used
  - Interpret number of twitches (0-4) and presence of fade
- DBS
  - Occasionally used
  - Interpret number of twitches (0-2) and presence of fade
- Tetanus
  - Commonly used
  - Interpret presence of fade either at 50 or 100 Hz for 5 seconds
- PTC
  - Rarely used
  - Interpret number of twitches after 5 second tetanus

Neuromuscular Function Monitoring

- Quantitative nerve monitor
  - Gold standard
  - Provides a measured TOF ratio
  - Monitors the ulnar nerve and adductor pollicis brevis
- Qualitative nerve monitor
  - Various modes: TOF, double burst stimulation (DBS), tetanus, post-tetanic count (PTC)
  - Most commonly used monitor
  - Monitors the ulnar nerve, facial nerve, and posterior tibial nerve

Monitoring Site

- Site matters
- Ulnar nerve is most studied site
  - Quantitative monitors use this site
  - Level of blockade correlates to oropharyngeal blockade
- Facial nerve is most convenient site
  - Level of blockade correlates to diaphragm blockade
- Posterior tibial nerve is an occasional site
  - Does not correlate well to ulnar nerve

Neostigmine Reversal

- Mainstay of neuromuscular blockade reversal for decades by inhibiting acetylcholinesterase
- Highly variable time to completely reverse neuromuscular blockade
- Associated with numerous muscarinic side effects: bradycardia, hypotension, bronchoconstriction, and excessive secretions. These are usually treated by concurrent administration of glycopyrrolate.

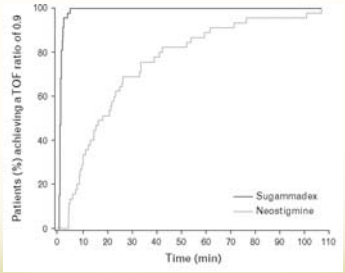
Sugammadex Dosing

- Shallow to moderate blockade
  - 2 mg/kg
- Profound blockade
  - 4 mg/kg
- Immediate reversal following RSI dose
  - 16 mg/kg

Sugammadex Reversal

- FDA approved in December 2015
- Currently used in ~70 countries with ~12 million patients receiving drug by mid 2015
- Poised to become the predominant reversal agent
- Studies for sugammadex have provided excellent data for neostigmine as well

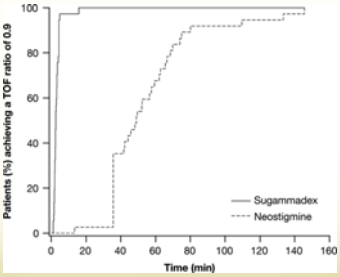
Moderate Blockade



Sugammadex Pharmacology

- Molecule is a cyclodextrin with a center cavity containing anionic character to bind and encapsulate steroid NMBs that have cationic character via their quaternary amine group
- 1:1 binding
- Not metabolized
- Renal excretion
- Elimination half life is ~2 hours

Profound Blockade



Immediate Reversal

Table 1. Time (min) from Start of Administration of Neuromuscular Blocking Agent to Recovery of T_1 to 10% and T_1 to 90%

	Treatment Group	
	Rocuronium + Sugammadex* (n = 55)	Succinylcholine Only (n = 55)
Recovery to T_1 10% (primary endpoint)		
Mean (SD)	4.4 (0.7)	7.1 (1.6)†
Median	4.2	7.1
Min–max	3.5–7.7	3.8–10.5
Recovery to T_1 90%		
Mean (SD)	6.2 (1.8)	10.9 (2.4)†
Median	5.7	10.7
Min–max	4.2–13.6	5.0–16.2

* Protocol-specified sugammadex administration at 3 min after the start of rocuronium administration (mean [SD] 3.1 [0.2]; range 2.7 to 4.2 min). † $P <$ 0.001 between treatment groups.

Sugammadex Adverse Events

- Hypersensitivity ~0.25%
  - Cutaneous manifestations
  - Sneezing
  - Rhinorrhea
  - Nausea/Vomiting
- Anaphylaxis <0.1%