Safety in The Operating Room: Updating Best Practices in Neuromuscular Blockade and Reversal

Michael R. England, MD

Senior Cardiac Anesthesiologist

Tufts Medical Center (TUSM)

Boston, MA 02111

Disclosures

- Michael R. England, M.D., declares that he serves on a speaker's bureau for Merck.
- This is a CME sponsored event
- No industry support or involvement

Learning Objectives

- Review commonly administered neuromuscular blocking (NMB) agents, their, history, purpose, and potential side effects.
- Examine current monitoring practice for administration and reversal of NMB agents
- Recommend pathways to minimize safety risks associated with residual paralysis.
- Discuss the ways to make Rapid Sequence Induction (RSI) “Safer”

Are you involved in operating room (OR) medication decisions?

A. Yes

B. No

In current clinical practice, how often is a train-of-four (TOF) monitor used routinely?

A. 5%

B. 10%

C. 50%

D. 100%

Is there any clinical difference between a Peripheral Nerve Stimulator (PNS) and an Accelerometer?

(Qualitative ***vs*** Quantitative monitoring)

A. No

B. Yes

When is a patient considered “fully reversed” after use of a NMB agent?

A. When they can squeeze your hand

B. When patients can sustain a head lift for 5 sec.

C. When you can feel four twitches on the TOF monitor

D. When the TOF ratio is >0.9%

What percentage of patients are inadequately reversed upon entry to the post-anesthesia care unit (PACU) after getting NMB agents?

A. 0%

B. 5%

C. 30-40%

D. >50%

Should all patients given a NMB be reversed in the operating room prior to extubation?

A. Yes

B. No

Succinylcholine (SDC) is the "safest" agent for a rapid sequence induction (RSI) for a "full stomach"?
Rather than 1.2 mg/kg rocuronium

A. Yes

B. No

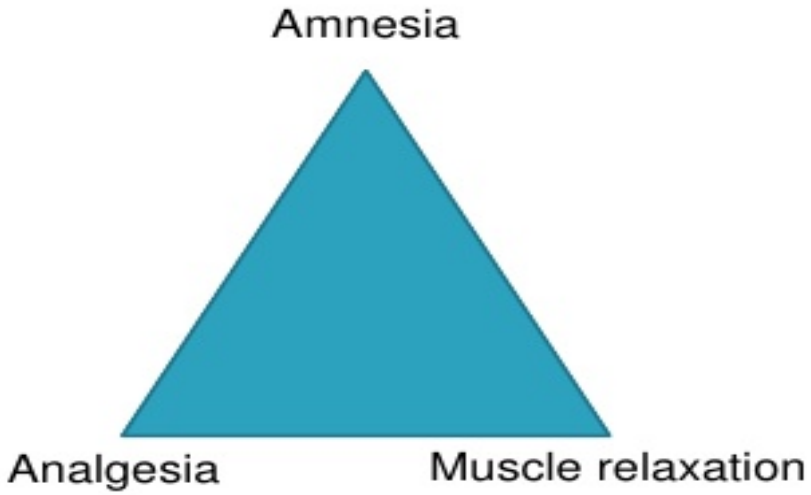
Boston, Massachusetts
October 19, 1846

"Boston Medical Library in the Francis A. Countway Library of medicine."
Used by permission.

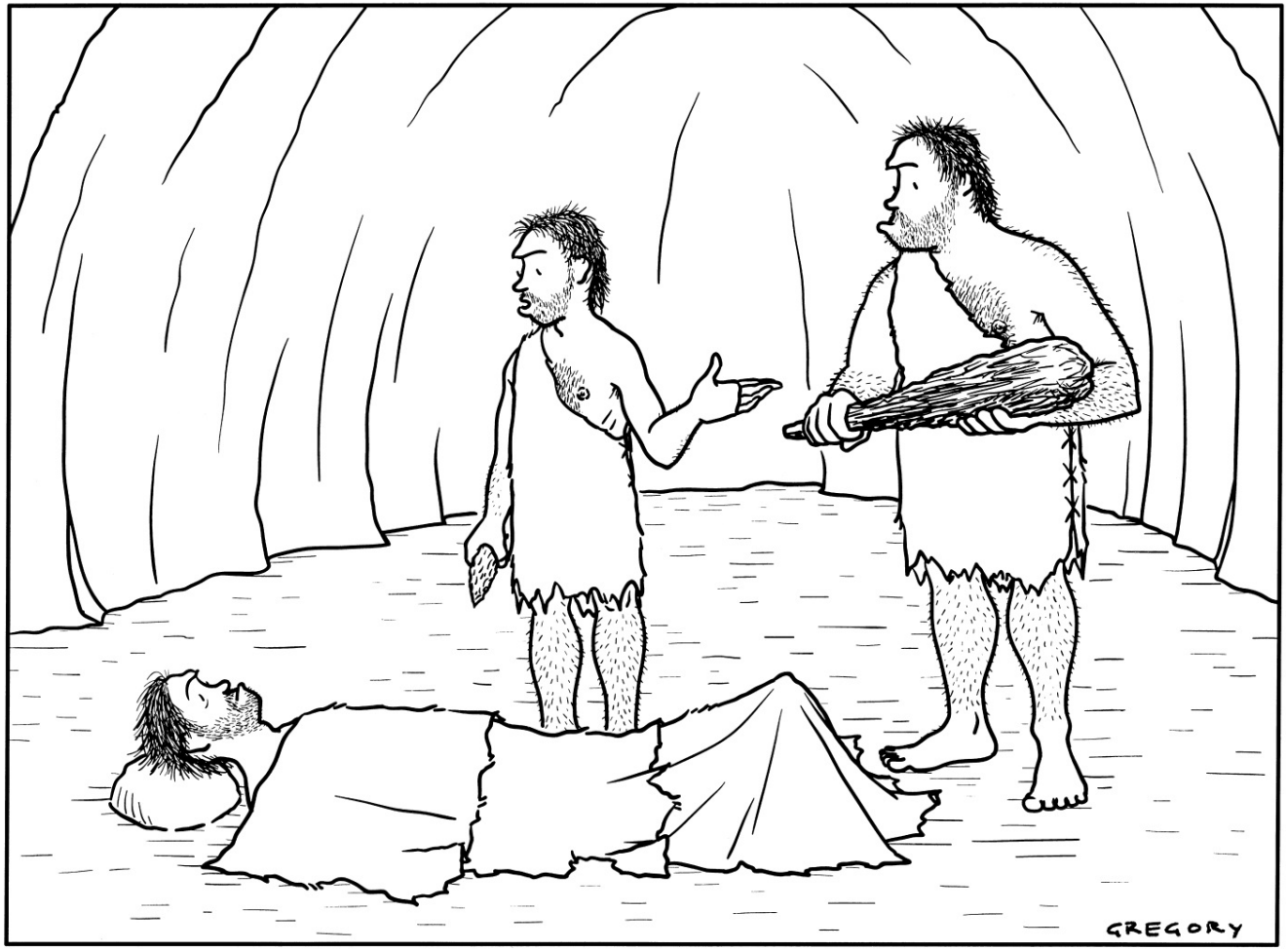
What is “anesthesia”?

Triad of Anaesthesia

- Triad of anaesthesia



From *The New Yorker* 1/14/08



"I'll be performing the operation, and this is the anesthesiologist."

What do we use to produce "anesthesia"?

- Amnesia
  - Sedatives/Hypnotics
    - Midazolam, propofol, inhalational agents
- Analgesia
  - Narcotics or "non-narcotics"
- Neuromuscular blocking (NMB) agents
  - Depolarizing – Succinylcholine (SDC)
    - Two acetylcholine (ACH) molecules
  - Non-depolarizing agents – large steroid moieties
    - Rocuronium, vecuronium
  - Non-depolarizing agents – benzylisoquinolines
    - Atracurium/cisatracurium, mivacurium (eliminated by Hoffman elimination)

History of Neuromuscular Blockade (NMB)

The first known use was by Amazon Natives using poison tipped arrows

- Active agent recognized as *d*- tubocurarine

First published use by Griffith in ANES. In 1942

- Wide spread in clinical practice 1943

Surgical death rates described thereafter by Beecher/Todd in 1954

- 1:2100 w/o NMB ***vs*** 1:370 with

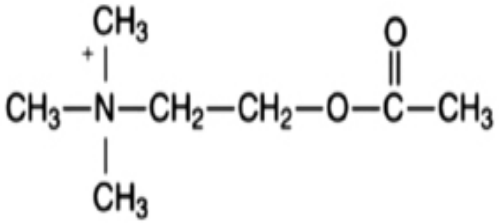
Muscle Relaxants

A major part of our anesthesia

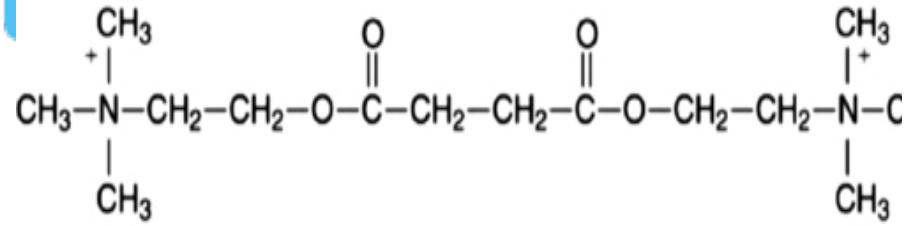
- Either depolarizing or non-depolarizing

quiver

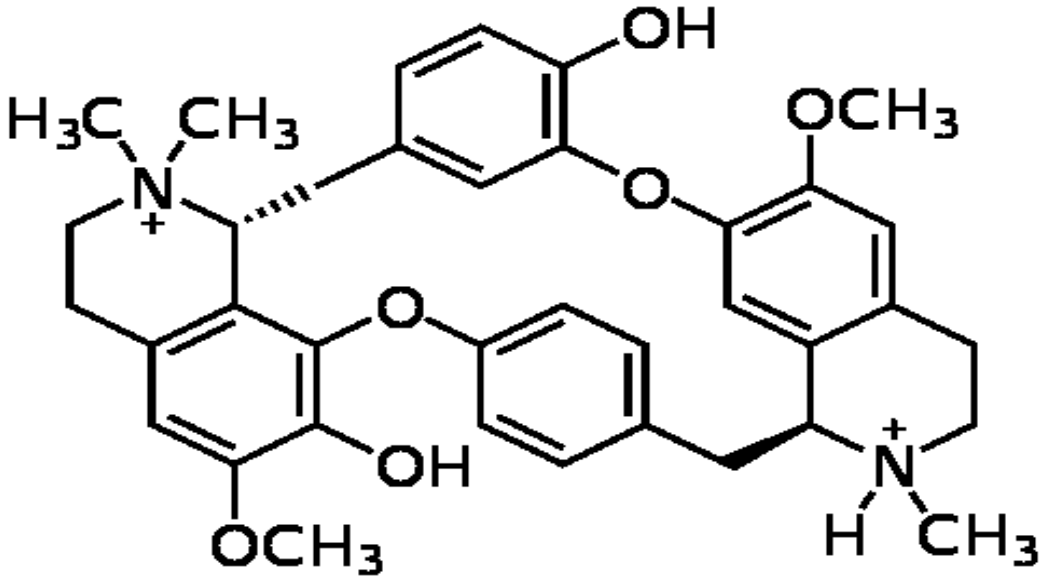
Structures



Acetylcholine

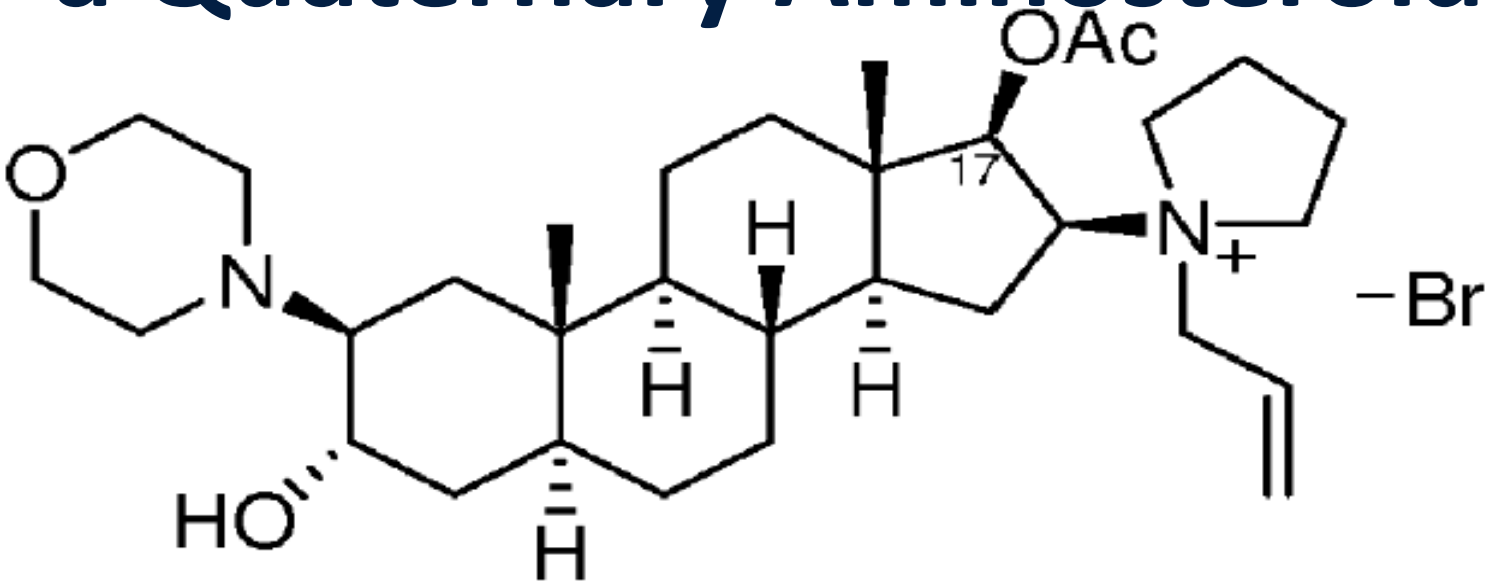


Succinylcholine



tubocurarine

Rocuronium
a Quaternary Aminosteroid



Rocuronium bromide

- Vecuronium analog
- Fast onset – intermediate acting to compete with ACH
- ED90 of 0.3 mg/kg
- ED90 is the dose required to produce 90% depression of the twitch response

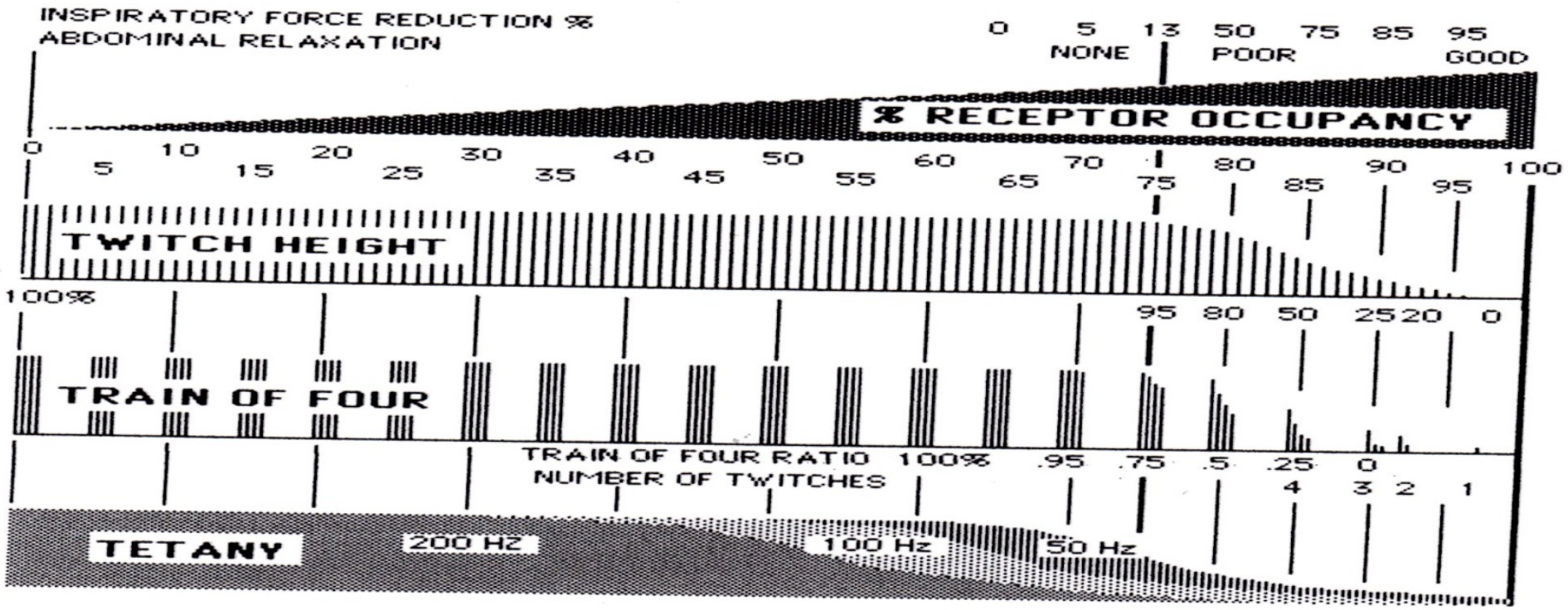
Monitoring the Neuromuscular Junction (NMJ)

Train-of Four (TOF)

Only used by 10% of caregivers! In US, Aus, New Zealand
20% Europe

Brull **ANES** 2017

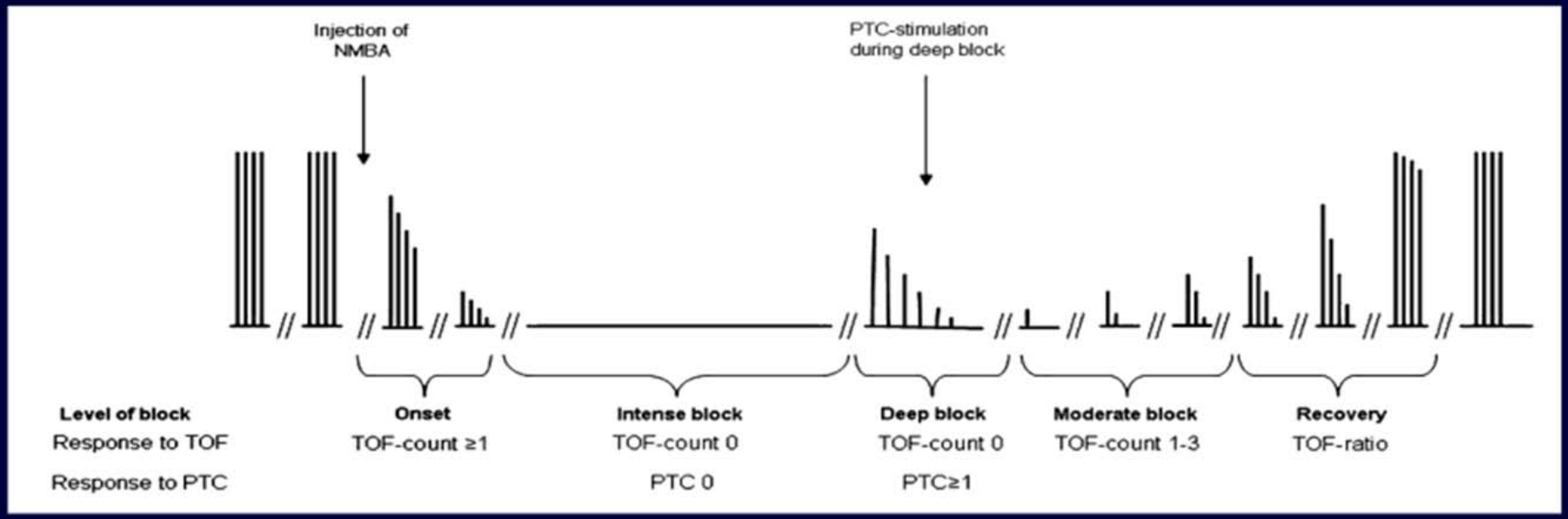
NMJ Receptor Blockade



Receptor occupancy and clinical responses

Neuromuscular Monitoring

- Qualitative
  - Peripheral nerve stimulator (PNS)
  - Train-of-four (TOF) count
  - Reappearance of T2
  - TOF fade
  - Post-tetanic count (PTC)
- Quantitative
  - TOF-Watch®
  - TOF ratio
  - TOF ratio: 0-1.0
  - Residual block: TOF ratio <0.9
  - T1 (first twitch) ratio



Fuchs-Buder, et al. Acta Anaesthesiol Scand. 2007;51:789-808.
NMBA=neuromuscular blocking agent.

Monitoring of the NMJ Accelerometer

How do we "reverse" the effects of neuromuscular blocking agents?

- If we are using a depolarizing agent
  - Depends on enzymatic elimination-first twitch appears- 7-9 mins
    - Or tincture of time if there is an enzyme deficiency
- If we are using a non-depolarizing agent
  - We have to wait until there is evidence of two twitches if we are using a TOF monitor (or an accelerometer)
    - Tactile quantification is lost at TOF >0.4%
    - Accelerometers will display the ratio of twitch heights
- Then we usually administer an

Should this continue to be the standard of care?

By reversing NMJ transmission in the state of organophosphate poisoning?

Signs and symptoms

Table 3. Signs And Symptoms Of Acute Organophosphate Poisoning

Muscarinic Manifestations

Ophthalmic: Conjunctival injection, lacrimation, miosis, blurred vision, diminished visual acuity, ocular pain

Respiratory: Rhinorrhea, stridor, wheezing, cough, excessive sputum, chest tightness, dyspnea, apnea

Cardiovascular: Bradydysrhythmias, hypotension

Dermal: Flushing, diaphoresis, cyanosis

Gastrointestinal: Nausea, vomiting, salivation, diarrhea, abdominal cramping, tenesmus, fecal incontinence

Genitourinary: Frequency, urgency, incontinence

Nicotinic Manifestations

Cardiovascular: Tachydysrhythmias, hypertension

Striated muscle: Fasciculations, twitching, cramping, weakness, paralysis

Central Nervous System Manifestations

Anxiety, restlessness, depression, confusion, ataxia, tremors, convulsions, coma, areflexia

Neostigmine

Brought to you by only one maker!

Now we “gotch ya”

cost?

New FDA Regulations

FDA Consumer Health Information
www.fda.gov/consumer

Generic Drugs Undergo Rigorous FDA Scrutiny

Perhaps you've had this experience: You go to your local pharmacy to fill a prescription from your doctor, and the pharmacist confirms there is a generic available.

"If it's a copy, it must not be as good," you think.

You would be wrong.

What are generic drugs, and how does the Food and Drug Administration ensure that they are as safe and effective as brand-name drugs?

Rigorous Standards

A brand-name drug is often patented to protect it from competition and thus to help the drug manufacturer recover the development costs. Several years later when the patent expires, other drug companies can copy the brand-name drug and seek FDA's approval for its generic version.

Today, more than 8 in 10 prescriptions filled in the United States are for generic drugs. The use of generic drugs is expected to grow over the next few years as a number of popular drugs come off patent.

Because generic drug makers are not required to repeat the clinical trials of new drugs and generally do not pay for advertising, marketing and promotion, generics are usually substantially less expensive than brand-name drugs. According to the Congressional Budget Office, generic drugs save consumers an estimated

An FDA scientist in the agency's Division of Product Quality Research evaluates beads used for coating a controlled-release generic drug product.

Generic Neostigmine

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INDICATIONS AND USAGE

BLOXIVERZ, a cholinesterase inhibitor, is indicated for the reversal of the effects of non-depolarizing neuromuscular blocking agents (NMBAs) after surgery in adults and pediatric patients of all ages.

Important Safety Information

CONTRAINDICATIONS

BLOXIVERZ is contraindicated in patients with known hypersensitivity to neostigmine. It is also contraindicated in patients with peritonitis or mechanical obstruction of the intestinal or urinary tract.

WARNINGS AND PRECAUTIONS

Atropine or glycopyrrolate should be administered prior to BLOXIVERZ to minimize risk of bradycardia.

BLOXIVERZ should be used with caution in patients with the following coexisting conditions as serious reactions may occur: coronary artery disease, cardiac arrhythmias, recent acute coronary syndrome or myasthenia gravis.

Neuromuscular dysfunction can occur if large doses of BLOXIVERZ are administered when neuromuscular blockade is minimal; reduce dose if recovery from neuromuscular blockade is nearly complete.

ADVERSE REACTIONS

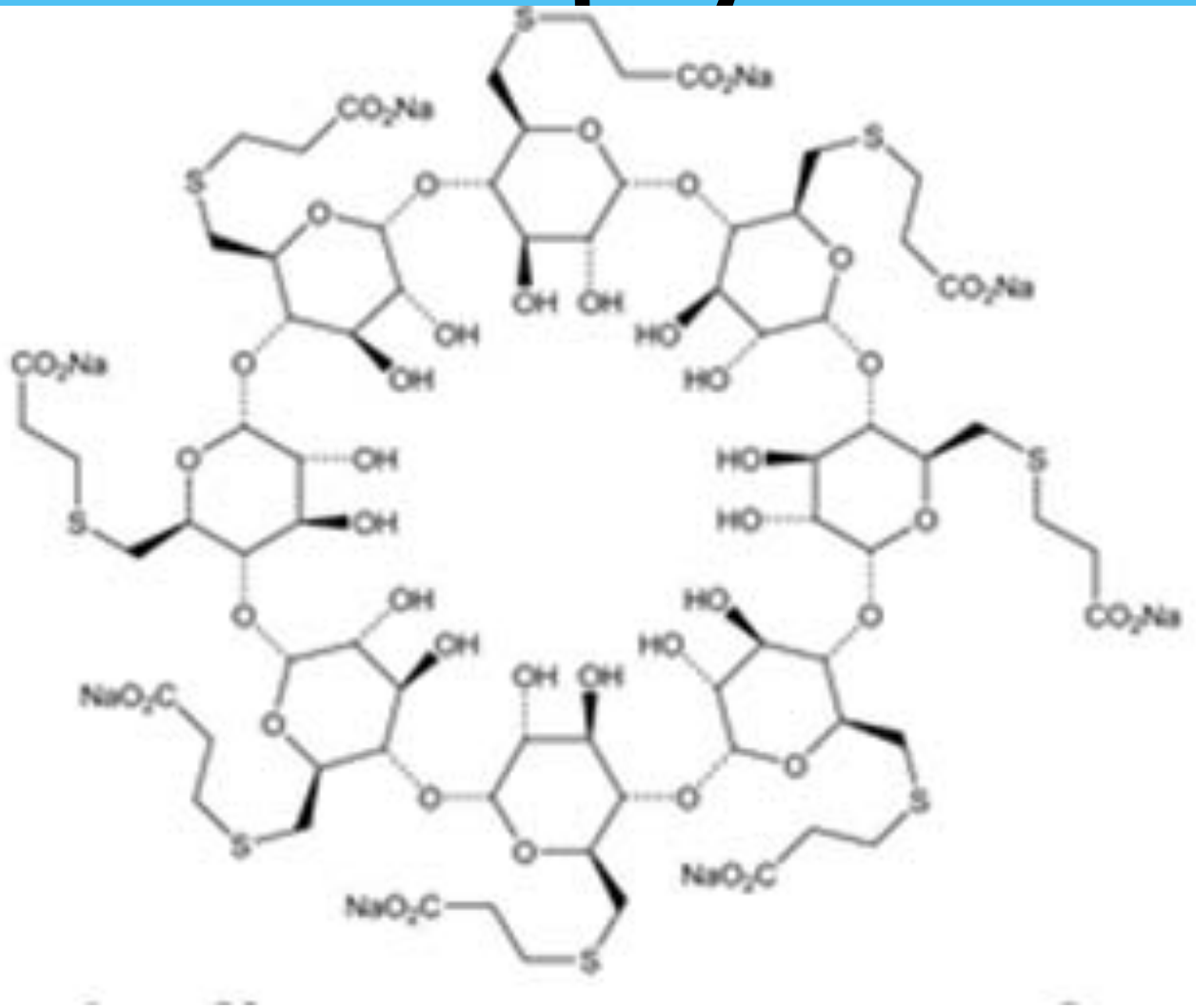
The most common adverse reactions during treatment are bradycardia, nausea and vomiting.

To report SUSPECTED ADVERSE REACTIONS, contact Éclat Pharmaceuticals at 1-877-622-2320 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Should this continue to be the standard of care?

- Are we really adequately monitoring the pharmacodynamics of our NMB agents?
  - Using the TOF correctly?
  - Are we keeping the patients too paralyzed in fear of appearing to let them move (signs of life)
    - Is this really a sign of a bad anesthetic?
  - What happens if surgery is stopped suddenly?
    - Can we adequately/predictably reverse our paralysis?
  - What if we can't intubate/ventilate after RSI?

Enter Sugammadex
A γ-cyclodextrin



-Rigid ring shaped sugars
-Outside is hydrophilic water soluble
-The hole in the middle of the ring is hydrophobic that permits lipophilic moieties to enter and become encapsulated

No affinity for benzoisoquinolinium NMB

Anesthesia Patient Safety Foundation Newsletter. 2016; 30:45-76.

Sugammadex

- It was developed to selectively bind rocuronium (fast, short acting, non-depolarizing steroid NMB agent)
  - It binds to vecuronium with much lower affinity
- It has no affinity for other NMB agents
  - SDC, mivacurium, atracurium, or cisatracurium
- First human studies in 2005
- Has been given to 6000 patients in trials

Anesthesia Patient Safety Foundation Newsletter. 2016; 30:45-76.

Sugammadex

- European Union approval in 2008
- FDA new drug application (NDA) in 2007
  - Concerns centered around safety
    - Re-exposure (hypersensitivity, anaphylaxis)- very low
    - Bleeding
    - Cardiac arrhythmias, prolonged QT interval
- In 2013, bleeding and cardiac issues resolved
- In 2014, reports demonstrated 1 patient met the anaphylaxis criteria after 16 mg/kg
  - Mechanism unclear – no tryptase or IgE, IgG

Anesthesia Patient Safety Foundation Newsletter. 2016; 30:45-76.

- FDA approval December 2015

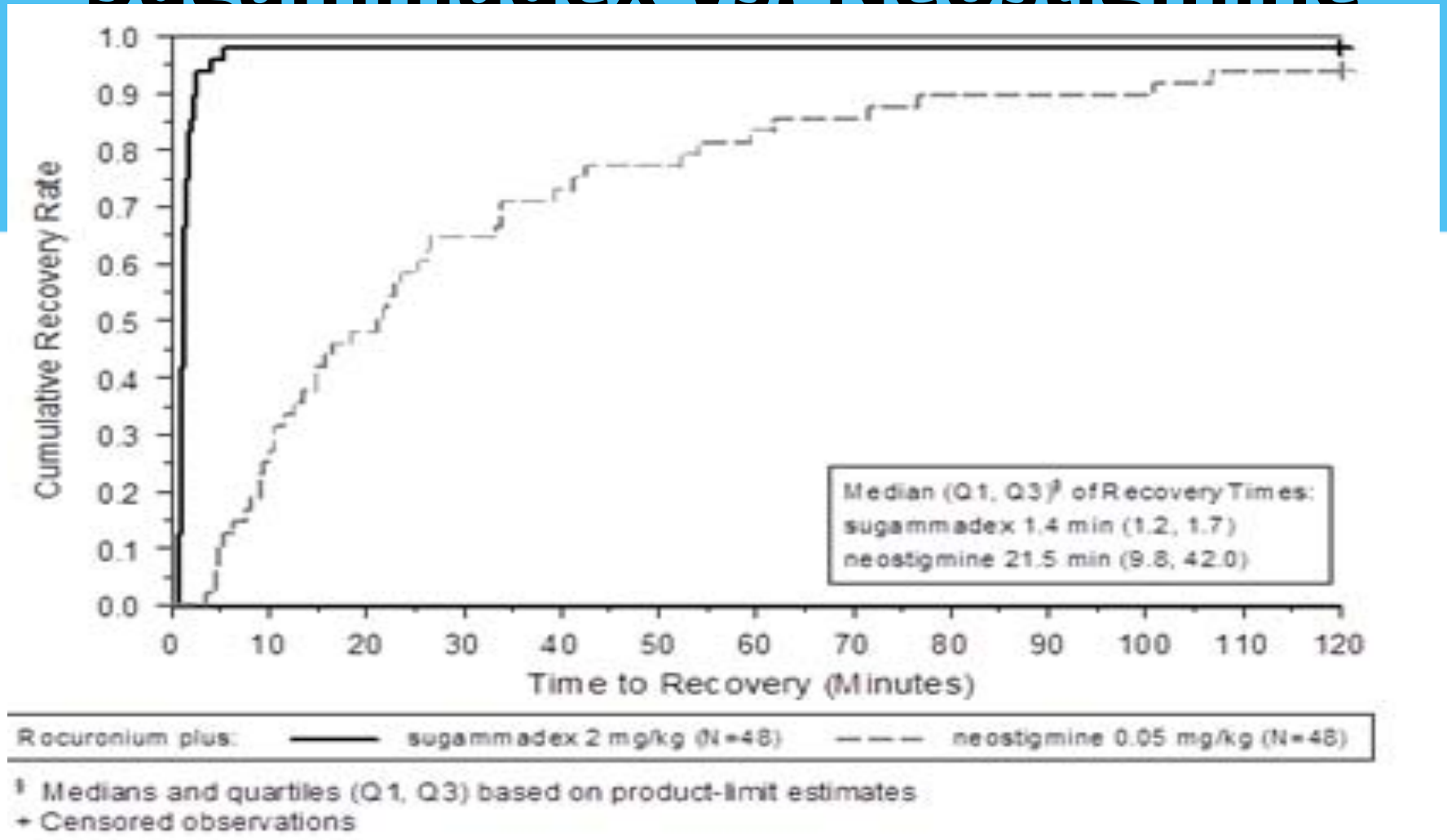
Sugammadex for Reversal of Neuromuscular Blockade

- Can reverse neuromuscular blockade
  - Moderate block 2 mg/kg (one or two twitches)
    - Mean time to recovery 1.5 minutes – TOF 0.9
    - 19 minutes for neostigmine
  - Deep blockade – 4 mg/kg (PTC of 1-2) in 3 minutes
  - Neostigmine is not able to do this
- Can reverse rocuronium dose 1.2 mg/kg
  - 16 mg/kg faster than spontaneous recovery from SDC

PTC=post-tetanic counts

Anesthesia Patient Safety Foundation Newsletter. 2016; 30:45-76.

Recovery Times
Sugammadex vs. Neostigmine



[1] Medians and quartiles (Q1, Q3) based on product-limit estimates
+ Censored observations

Jones RK et al. *Anesthesiology*. 2008; 109:816-24.

Patient Case

25 year-old male scheduled for laparoscopic appendectomy

Past Medical History (PMH) not an issue

Body Mass Index (BMI) 45 kg/m2

Mallampatti 3 (uvula not well visualized)

Case Raises Issues

- The patient needs their airway secured as quickly as possible to minimize aspiration risk
- What is the best agent to accomplish this?
  - For many succinylcholine, but there are issues
    - Myalgia, hyperkalemia
  - Now rocuronium 1.2 mg/kg provides intubating conditions as fast as succinylcholine
- What to do if we can't intubate/ventilate?
  - Now which is better?

Time for a Decision
Which drug would you suggest?

How many people would reach for?

A. Succinylcholine

B. Rocuronium (1.2 mg/kg)

Time to Recovery for First Twitch 10% of Baseline

	Treatment Regimen	
	Rocuronium 1.2 mg/kg and sugammadex 16 mg/kg	Succinylcholine 1 mg/kg
Number of patients	55	55
Mean time in minutes (SD)	4.4 (0.7)	7.1 (1.6)
Median time in minutes (Range)	4.2 (3.5-7.7)	7.1 (3.8-10.5)

Lee C et al. *Anesthesiology*. 2009; 110:1020-5.

Advantages of Sugammadex vs. Neostigmine/Glycopyrrolate

- It will permit flexible administration of NMB agent
  - Maintaining deep blockade until end of surgery
    - Reverse quickly (with one PTC) 4 mg/kg
    - Reliably (not possible with neostigmine)
- Risk of postoperative residual neuromuscular blockade (RNMB) in PACU using sugammmadex
  - Has been shown to be reduced
    - From 43% to 6%

Anesthesia Patient Safety Foundation Newsletter. 2016; 30:45-76.
Brueckmann B et al. *Br J Anaesth*. 2015; 115:743-51.

Adverse Reactions to Sugammadex

Body system	2 mg/kg (*n*=895)	4 mg/kg (*n*=1921)	16 mg/kg (*n*=98)	Placebo (*n*=544)
Incision site pain	6%	6%	4%	1%
Procedural complication	1%	1%	8%	1%
Airway issues	1%	1%	9%	1%
Anesthesia complications	1%	1%	9%	<1%
RNMB (PACU)	0%	<1%	2%	0

Bridion (sugammadex) prescribing information. Merck and Co., Inc. 2016 Sept.

Adverse Reactions to Sugammadex

Body system	2 mg/kg	4 mg/kg	16 mg/kg	Placebo
Nausea	23%	26%	23%	23%
Vomiting	11%	12%	15%	10%
Abdominal Pain	5%	4%	6%	3%
Flatulence	2%	3%	1%	2%
Dry mouth	1%	<1%	2%	0
Pain	48%	52%	36%	38%
Pyrexia	9%	6%	5%	3%

Bridion (sugammadex) prescribing information. Merck and Co., Inc. 2016 Sept.

Concerns with Sugammadex

- Is incompatible with
  - Verapamil
  - Ondansetron
  - Ranitidine
- Most common (dose-related) hypersensitivity reactions
  - Nausea
  - Pruritus
  - Urticaria

Bridion (sugammadex) prescribing information. Merck and Co., Inc. 2016 Sept.

Pharmacokinetics of Sugammadex

- No metabolism
- Renal clearance = glomerular filtration rate (GFR)(88 mL/min)
- Plasma half-life = 2 hours (>90% gone in 24 hr)
- Linear pharmacokinetics (PK)(dose range 0.1-96 mg/kg)
- Low potential for drug-drug interactions
- Similar PK for surgical/non-surgical patients
- No dose adjustment for age, gender, weight
- Not recommended for patients in renal failure

Bridion (sugammadex) prescribing information. Merck and Co., Inc. 2016 Sept.

Re-dosing of Sugammadex Normal GFR

Minimal Waiting time	NMB agent to be administered
Five minutes	1.2 mg/kg rocuronium
Four hours	0.6 mg/kg rocuronium 0.1 mg/kg vecuronium

- When 1.2 mg/kg of rocuronium is given within 30 minutes sugammadex
- Onset of NMB may be delayed up to 4 minutes and duration shortened by 15 minutes
- If 16 mg/kg used, wait 24 hours!

Bridion (sugammadex) prescribing information. Merck and Co., Inc. 2016 Sept.

Progesterone Levels after Sugammadex

- In vitro binding studies indicate that sugammadex may bind to progesterone
- It may be equivalent to missing a dose of birth control pills (BCP)
- It is suggested that if a BCP is taken on the day sugammadex is given, a back-up method of birth control be used for up to 7 days
- In the case of non-oral hormonal contraceptives, use additional methods to prevent pregnancy for 7 days!

Bridion (sugammadex) prescribing information. Merck and Co., Inc. 2016 Sept.

To Prevent Unwanted Pregnancy

You have been given a drug called sugammadex.

Sugammadex is an anesthesia drug that helps restore muscle strength after surgery. Sugammadex can interfere with progestin-based birth control. This includes many birth control pills, injectable hormonal birth control such as Depo-Provera injection and hormonal Intra-uterine systems, implants, or a vaginal ring. This effect is similar to missing one oral contraceptive pill. **To prevent unintended pregnancy, you should use a backup method of birth control for one week (7 days).**

Tufts Medical Center Patient Information.

Answers to Questions

- In current practice only 10% of caregivers use the TOF
- A patient is fully “reversed” when TOF ratio is >0.9%
- 30-40% patients entering the PACU have evidence of residual blockade
- Probably 1.2 mg/kg is “SAFER” because it is possible to reverse using 16 mg/kg sugammadex
  - No reversal possible using SDC 1 mg/kg – must wait 9 minutes for one twitch to appear!

Should all patients be reversed?

YES

Glenn Murphy ANESTHESIOLOGY 10/16

EDITORIAL VIEWS

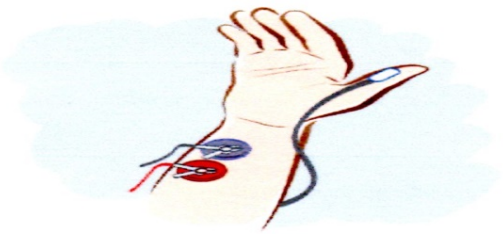
"To Reverse or Not To Reverse?"

The Answer Is Clear!

Glenn S. Murphy, M.D., Aaron F. Kopman, M.D.

BY the late 1980s, it was well recognized that undetected postoperative residual neuromuscular block (PRNB) was a common occurrence in most postanesthesia care units (PACUs).[1–4] However, an editorial in 1989 noted that there was little, if any, objective evidence to validate the hypothesis that PRNB was associated with long-term or even transient adverse respiratory outcomes.[5] In the two and a half decades since the editorial by Miller[5] was published, outcome data regarding this important patient safety issue have slowly accumulated, but the relevant database remains quite sparse. In this issue of ANESTHESIOLOGY, Bulka *et al.*[6] provide an important addition to the small list of studies that attempt to examine the long-term consequences of PRNB. They report two main findings: (1) the use of neuromuscular blocking agents (NMBAs) was associated with a higher absolute rate of postoperative pneumonia (POP) when compared to matched cases where patients did not receive relaxants and (2) failure to reverse NMBAs at the end of surgery was associated with a 2.25-fold increase in the incidence of POP. Why should these findings be less than surprising?

Bulka *et al.*[6] noted that the incidence rate ratio (1.79) for POP was significantly higher in patients who received NMBAs. This observation is consistent with the findings from several large database investigations, which have described an association between intraoperative NMBA use and major morbidity and mortality. More than 60 yr ago, Beecher and Todd[7] reported that the risk of death related to anesthesia was six times higher in patients receiving NMBAs compared to those administered no muscle relaxants. An analysis of data collected over a 10-yr period (1967 to 1976) involving 240,483 anesthetics revealed that "respiratory inadequacy after myoneural blockade" was the second most common cause of death after surgery.[8] Similarly, a study from Great Britain reported that postoperative respiratory failure secondary to dosing of NMBAs was a primary cause of mortality.[9] In a large prospective study, the use of the long-acting NMBA pancuronium entailed a higher risk of postoperative pulmonary complications.[10] More recent studies reported that patients administered NMBAs had a higher risk of postoperative desaturations and need for reintubation[11] and that those given high doses of NMBAs had an increased risk of postoperative respiratory complications.[12] The increased incidence of morbidity and mortality reported in patients administered NMBAs is likely secondary to PRNB. Incomplete neuromuscular recovery during a vulnerable postoperative period (between tracheal extubation and achieving a train-of-four [TOF] ratio of less than 0.9 in the PACU) may impair upper airway patency, protective airway reflexes, breathing, swallowing, and coughing, resulting in an increased risk of significant respiratory events (like POP) and death.



"The hazards of postoperative residual neuromuscular block are well-documented; reversal of neuromuscular blocking agents should be routine."

Data demonstrating an association between failure to reverse neuromuscular blockade and adverse postoperative outcomes are less certain. A large case–control database investigation revealed that the primary anesthetic management characteristic associated with a reduction in mortality and coma was reversal of the effects of NMBAs.[13] In a

References ANESTHESIOLOGY 1/17

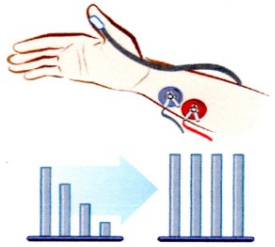
Innovative Disruption in the World of Neuromuscular Blockade

What Is the "State of the Art?"

Mohamed Naguib, M.B., B.Ch., M.Sc., F.C.A.R.C.S.I., M.D., Ken B. Johnson, M.D.

CME This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

SUGAMMADEX represents an innovative disruption in drug technology. The recent approval of sugammadex by the Food and Drug Administration provides us with an opportunity to revisit the "state of the art" and emphasize important nuances in the administration, monitoring, and reversal of neuromuscular blockade. To that end, in this issue of ANESTHESIOLOGY, Brull and Kopman[1] review the status of monitoring and reversal of neuromuscular blockade, highlight persistent concerns with residual neuromuscular block, and address approaches on how to minimize them. This editorial highlights a few of the more important clinical implications of this review to include practice considerations of sugammadex *versus* neostigmine, the importance of monitoring neuromuscular blockade, clinically relevant drug interactions, adverse effects, and the pharmacoeconomics of sugammadex.



"...we encourage the American Society of Anesthesiologists committee on standards and practice parameters to consider adding a monitoring device ... anytime a neuromuscular blocking drug is administered."

Why Use Sugammadex When I Can Get by with Neostigmine?

Sugammadex, a modified γ-cyclodextrin, is highly water soluble with a hydrophobic cavity large enough to encapsulate steroidal neuromuscular blocking drugs. The reversal activity of sugammadex is selective for steroidal neuromuscular blocking drugs (rocuronium > vecuronium >> pancuronium). Sugammadex has a little to no affinity for binding to benzylisoquinolinium neuromuscular blockers. The affinity of sugammadex for rocuronium is approximately 4,700 times that of atracurium.[2]

There are many potential applications of sugammadex of interest to anesthesiologists. The main advantages of sugammadex over neostigmine are its predictability and its ability to extend the range of neuromuscular blockade reversal. Reversal of residual competitive neuromuscular blockade by cholinesterase inhibitors has its limitations, as outlined by Drs. Brull and Kopman.[1] Neostigmine provides reversal for minimal, light (shallow), and moderate blockade. Sugammadex extends reversal capability, and in recommended doses of 2 to 16 mg/kg, it is capable of reversing any depth of neuromuscular block induced by rocuronium (from moderate to profound block) to a train-of-four ratio of more than or equal to 0.9 within 3 min. This has been and will continue to be a "game changer" for many patients who suffer from prolonged neuromuscular blockade. Sugammadex is also advantageous in that it does not have any cholinergic side effects that require the coadministration of an anticholinergic agent. However, the administration of sugammadex has been associated with life-threatening bradycardia that may require administration of anticholinergic agents.[3] Hypotension, ST-segment elevation unresponsive to vasopressors and anticholinergic drugs, and even cardiac arrest have been reported after

Image: John Ursino, ImagePower Productions.

Corresponding article on page 173.

Accepted for publication May 23, 2016. From the Department of General Anesthesia, Anesthesiology Institute, Cleveland Clinic, Cleveland, Ohio (M.N.); and Department of Anesthesiology, University of Utah, Salt Lake City, Utah (K.B.J.).

REVIEW ARTICLE

Deborah J. Culley, M.D., Editor

Current Status of Neuromuscular Reversal and Monitoring

Challenges and Opportunities

Sorin J. Brull, M.D., F.C.A.R.C.S.I. (Hon), Aaron F. Kopman, M.D.

CME This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

ABSTRACT

Postoperative residual neuromuscular block has been recognized as a potential problem for decades, and it remains so today. Traditional pharmacologic antagonists (anticholinesterases) are ineffective in reversing profound and deep levels of neuromuscular block; at the opposite end of the recovery curve close to full recovery, anticholinesterases may induce paradoxical muscle weakness. The new selective relaxant-binding agent sugammadex can reverse any depth of block from aminosteroid (but not benzylisoquinolinium) relaxants; however, the effective dose to be administered should be chosen based on objective monitoring of the depth of neuromuscular block.

To guide appropriate perioperative management, neuromuscular function assessment with a peripheral nerve stimulator is mandatory. Although in many settings, subjective (visual and tactile) evaluation of muscle responses is used, such evaluation has had limited success in preventing the occurrence of residual paralysis. Clinical evaluations of return of muscle strength (head lift and grip strength) or respiratory parameters (tidal volume and vital capacity) are equally insensitive at detecting neuromuscular weakness. Objective measurement (a train-of-four ratio greater than 0.90) is the only method to determine appropriate timing of tracheal extubation and ensure normal muscle function and patient safety. (ANESTHESIOLOGY 2017; 126:173-90)

"We cannot solve our problems with the same thinking we used when we created them."

Albert Einstein

IT is widely recognized that the introduction of neuromuscular blocking agents into clinical care has revolutionized surgery and facilitated significant medical advances in the last century. In their 2015 article, Game changers: the 20 most important anesthesia articles ever published, Barash *et al.*[1] list the seminal article by Griffith and Johnson[2] on the use of curare in general anesthesia as number 13. Appropriately, the other "top-20 contender" article is the study by Beecher and Todd[3] of surgical deaths during anesthesia that, although rebutted at the time, features a "special discussion of muscle relaxants (curare)." In the article, the authors cite a mortality rate of 1:2,100 anesthetics that did not include the use of curare and a mortality rate of 1:370 when curare was used.[3] Significant solutions to complex problems in medicine often introduce new and unintended clinical problems, and the introduction of neuromuscular blocking agents (NMBAs) is no exception.

Side Effects of Muscle Relaxant Drugs—Residual Block

Incomplete recovery from NMBAs (residual block) after anesthesia and surgery continues to be a common problem in the postanesthesia care unit (PACU). Despite the routine use of anticholinesterase reversal agents, between 20% and 40% of patients continue to arrive in the PACU with objective evidence of residual NMBAs.[4–8] In the past year alone, multiple investigations have demonstrated that residual NMBAs is an important patient safety issue,[7–10] and multiple letters,[11] surveys,[8] and editorials[12,13] have called for a solution to this

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In Conclusion

- Sugammadex
  - May not be more expensive than the combination of
    - Neostigmine/glycopyrrolate
    - Does not share the side effect profile of neostigmine/glycopyrrolate
  - Can reliably reverse a moderate and deep blockade with less side effects and residual paralysis
  - This will alter NMB agent administration!
- Use carefully in situations where GFR is low

Dose for pre-intubation and timing/type of NMB