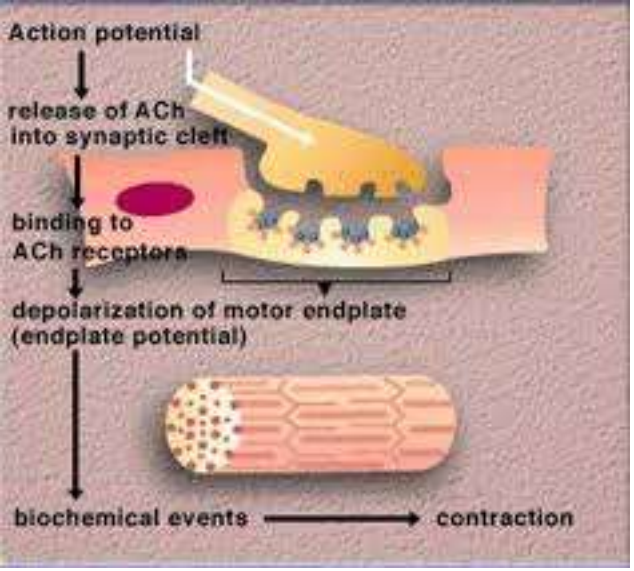
A.O.U. "Policlinico-V.Emanuele" di Catania
Scuola di Specializzazione in Anestesia e Rianimazione
U.O.C. Anestesia e Terapia Intensiva
Direttore: Prof.ssa M. Astuto

RISK MANAGEMENT DEL BLOCCO NEUROMUSCOLARE

SOCIETÀ ITALIANA DI FARMACIA OSPEDALIERA E DEI SERVIZI FARMACEUTICI DELLE AZIENDE SANITARIE

Paolo Murabito

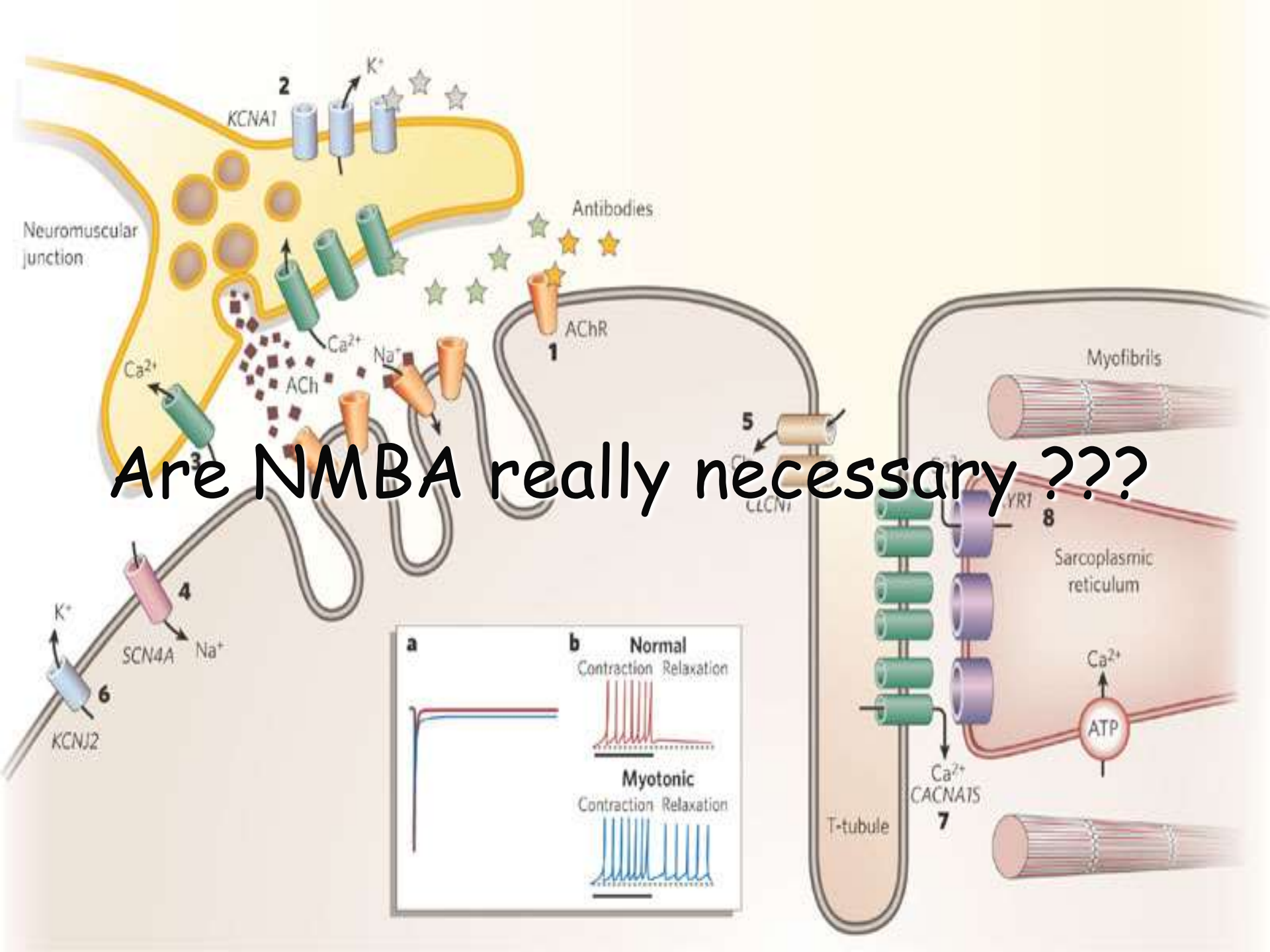


INTRODUCTION

Neuromuscolar blocking agents are potentially dangerous drugs when not safely managed.

The reversal of neuromuscolar activity can occur spontaneously (after a certain lack of time) or with the use of reversal agents.

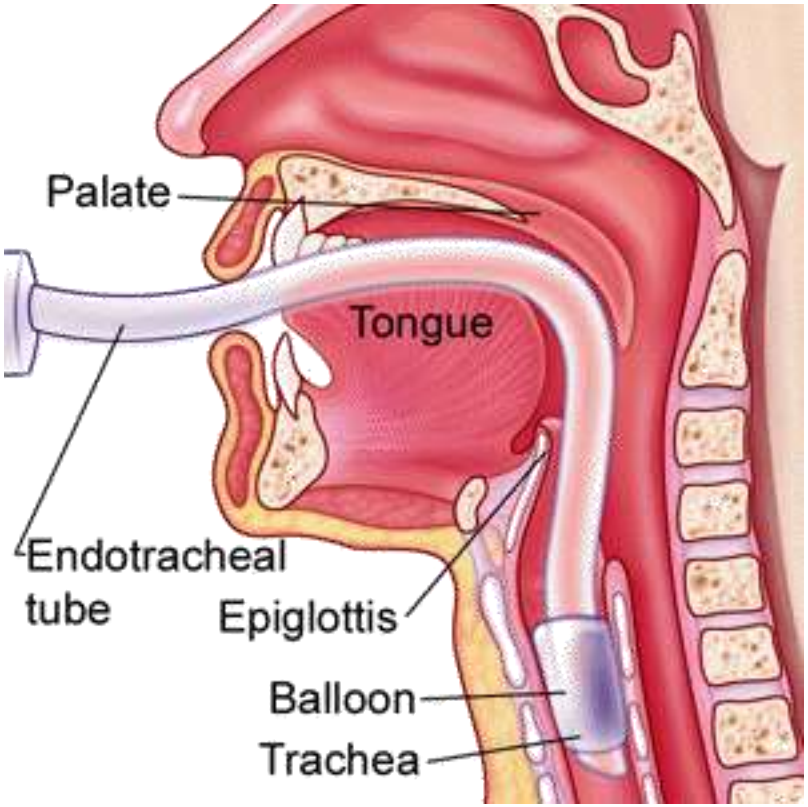
Neuromuscolar activity must be completely reversed before proceeding with estubation.



Are NMBA really necessary ???

SURGICAL GOOD VISION

AIRWAY MANAGEMENT



MECHANICAL VENTILATION

Anesthesiology 2003; 98:1049–56

Laryngeal Morbidity and Quality of Tracheal Intubation

A Randomized Controlled Trial

Thomas Mencke, M.D., Mathias Echternach, M.D.,† Stefan Kleinschmidt, M.D.,* Philip Lux,‡ Volker Barth, M.D.,† Peter K. Plinkert, M.D.,§ Thomas Fuchs-Buder, M.D.‖*

Table 1. Scoring Conditions for Tracheal Intubation

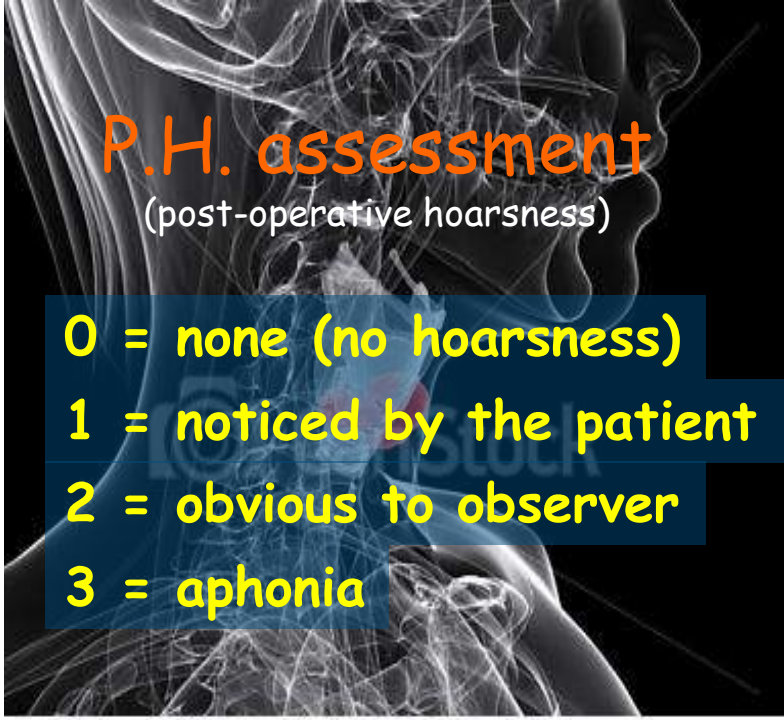
	Intubation Scores		
	Clinically Acceptable		Clinically Not Acceptable
Variable	Excellent	Good	Poor
Laryngoscopy	—	—	—
Jaw relaxation	Relaxed	Not fully	Poor
Resistance to laryngoscope	None	Slight	Active
Vocal cords	—	—	—
Position	Abducted	Intermediate	Closed
Movement	None	Moving	Closing
Reaction to tube insertion or cuff inflation	—	—	—
Movement of limbs	None	Slight	Vigorous
Coughing	None	Slight	Sustained

Intubation conditions: excellent = all qualities are excellent; good = all qualities are excellent or good. Excellent and good intubation conditions are summarized as clinically acceptable intubation conditions.

Table 4. Intubating Conditions and Intubating Scores

	Atracurium (n = 37)	Saline (n = 36)	P
Intubation conditions	—	—	—
Cormack grades	1 (1–2)	1 (1–2)	0.613
Time of intubation (s)	26 (10–106)	29 (7–90)	0.920
Attempts (n)	1 (1–3)	1 (1–3)	0.919
Intubation scores	—	—	—
Excellent	16	2	<0.001
Good	19	22	0.55
Poor	2	12	0.006
Clinically acceptable	35	24	0.006
Non-excellent	21	34	<0.001

Values are median and range (intubating conditions) or numbers.



© Can Stock Photo - csp4231872

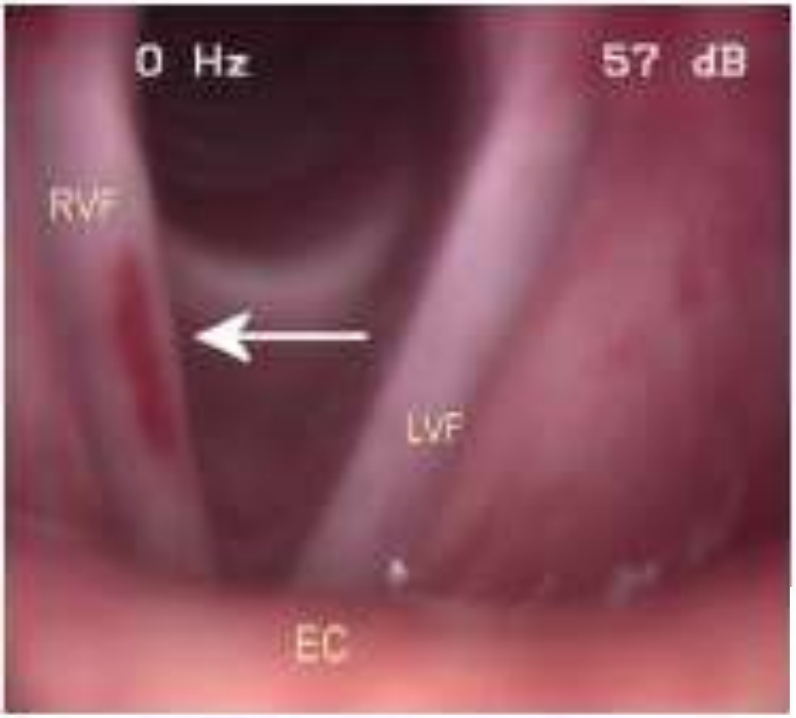
Table 5. Incidence of Postoperative Hoarseness and Vocal Cord Sequelae

	Postoperative Hoarseness			Vocal Cord Sequelae		
	Atracurium (n = 37)	Saline (n = 36)	P	Atracurium (n = 37)	Saline (n = 36)	P
PACU	6	13	0.1	NA	NA	—
At 24 h	0	6	0.01	3	15	0.002
At 48 h	0	4	0.05	NA	NA	—
At 72 h	0	1	0.5	1	8	0.014
>72 h	0	1	0.5	0	2	0.25
Days*	6	25	<0.001	5	50	<0.001
Patients	6	16	0.02	3	15	0.002

Values are shown as numbers of patients (n).

* Days = number of days with PH or VCS. PH was first assessed in the PACU and thus, the day of surgery was takes as the first day with PH. VCS was first assessed at 24 h and thus, postoperative day 1 was taken as the first day with VCS. † Patients: number of patients with PH or VCS.

PACU = postanesthesia care unit; PH = postoperative hoarseness; VCS = vocal cord sequelae; NA = not assessed.



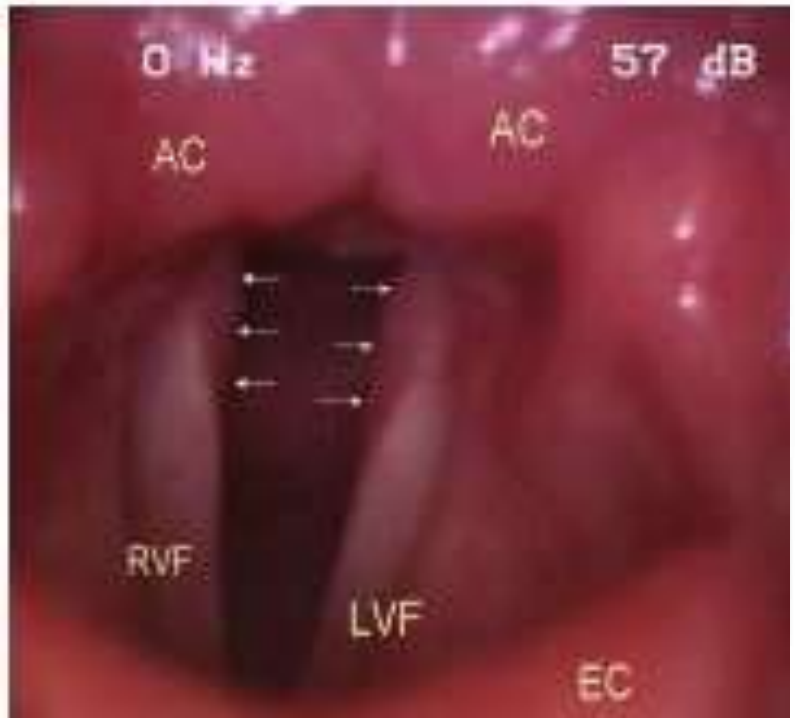
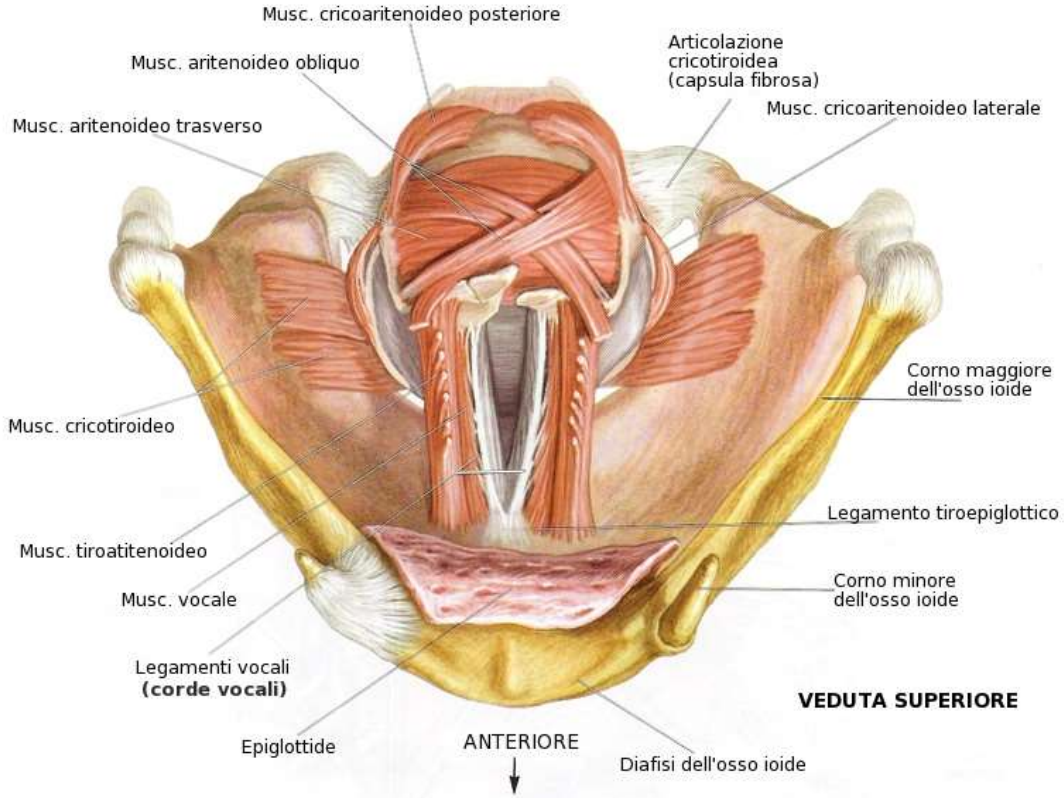


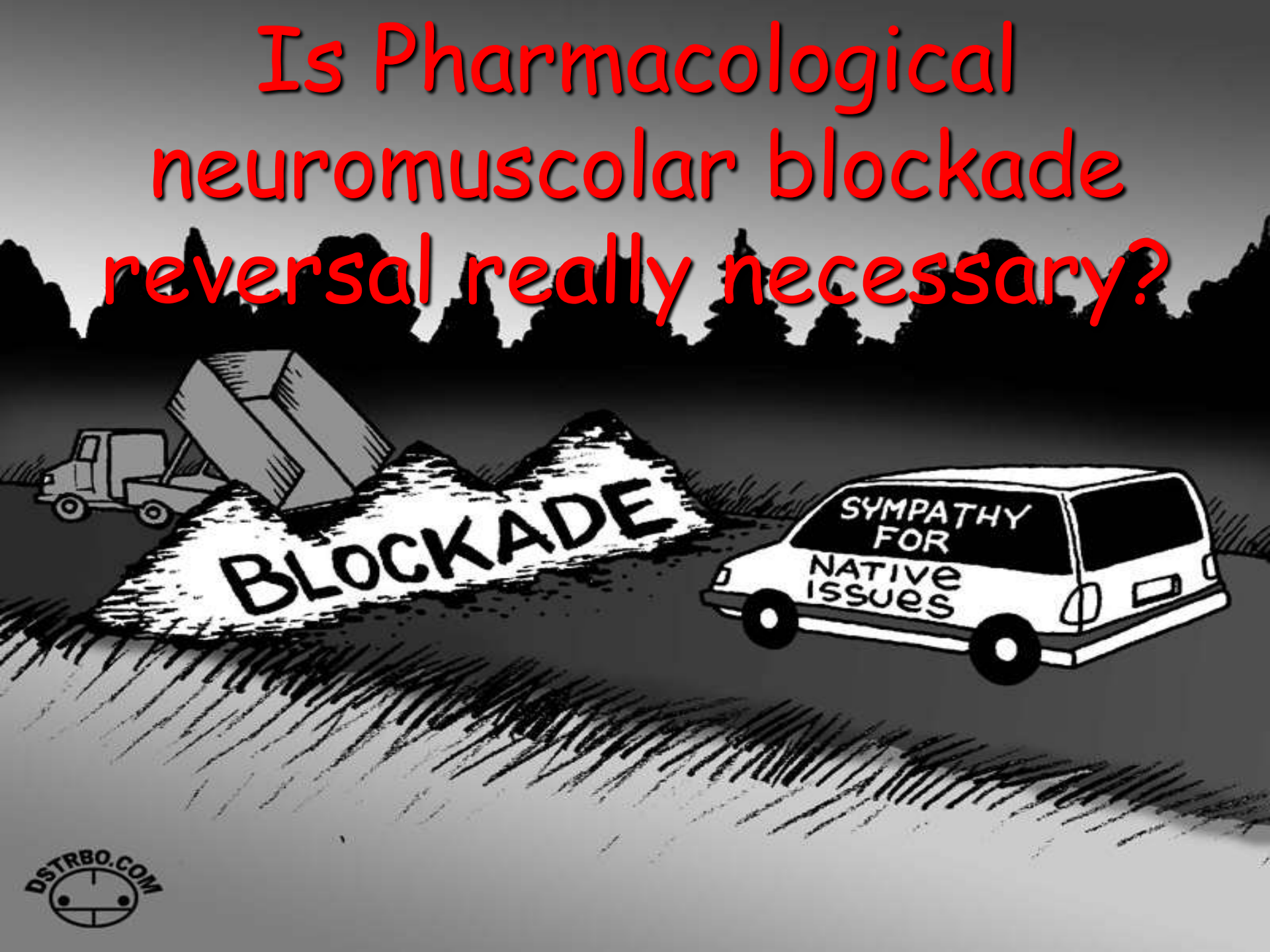
Table 6. Vocal Cord Sequelae: Stroboscopic Findings

	Atracurium (n = 37)	Saline (n = 36)	*P*
Unilateral	2	11	0.030
Left	1	8	0.047
Right	1	3	0.340
Bilateral	1	4	0.183
Morphology	—	—	—
Hematoma	1	10	0.008
Thickening of mucosa	3	6	0.31
Granuloma	0	2	0.24

Values are shown as numbers of patients (n).



Is Pharmacological neuromuscolar blockade reversal really necessary?



CLINICAL INVESTIGATIONS

Anesthesiology 2003; 98:1042–8

Residual Para… Dose of Nond… Intermediate …

Bertrand Debaene, M.D., B…*

Anaesthesia, 2007, **62**, pages 12–17 doi:10.1111/j.1365-2044.2006.04862.x

Incidence and duration of residual paralysis at the end of surgery after multiple administrations of cisatracurium and rocuronium

Anesthesiology 2008; 109:363–4

Undetected Resi… Consequences

PERIOPERATIVE MEDICINE

Anesthesiology 2008; 109:389–98

Intraoperative Acceleromyographic Monitoring Reduces the Risk of Residual Neuromuscular Blockade and Adverse Respiratory Events in the Postanesthesia…

CLINICAL CONCEPTS AND COMMENTARY

Anesthesiology 2010; 112:1013–22

teven B. Greenberg, M.D.,†

Residual Paralysis after Em…

Benoît Plaud, M.D., Ph.D.,* Bertrand Debaene, M…
François Donati, Ph.D., M.D., F.R.C.P.C.,‡ Jean…

Anesthesiology
2000; 92:977–84

The Incidence and Mechanisms of Pharyngeal and Upper Esophageal Dysfunction in Partially Paralyzed Humans

Pharyngeal Videoradiography and Simultaneous Manometry after Atracurium

Eva Sundman, M.D., Hanne Witt, M.D., Ph.D.,† Rolf Olsson, M.D., Ph.D.,† Olle Ekberg, M.D., Ph.D.,‡ Richard Kuylenstierna, M.D., Ph.D.,§ Lars I. Eriksson, M.D., Ph.D.‖*

Not only……

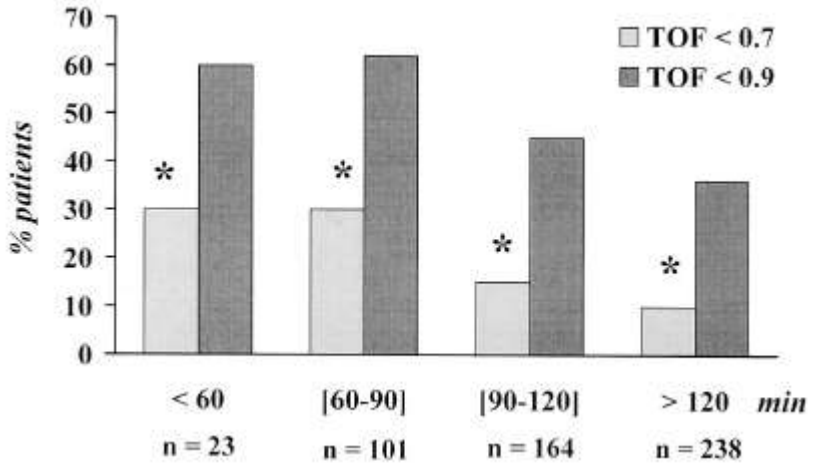
P.O.R.C. (POST-OPERATIVE RESIDUAL CURARIZATION)

Residual curarizzation means the insufficient recovery of the neuromuscolar function in an estubated patient.

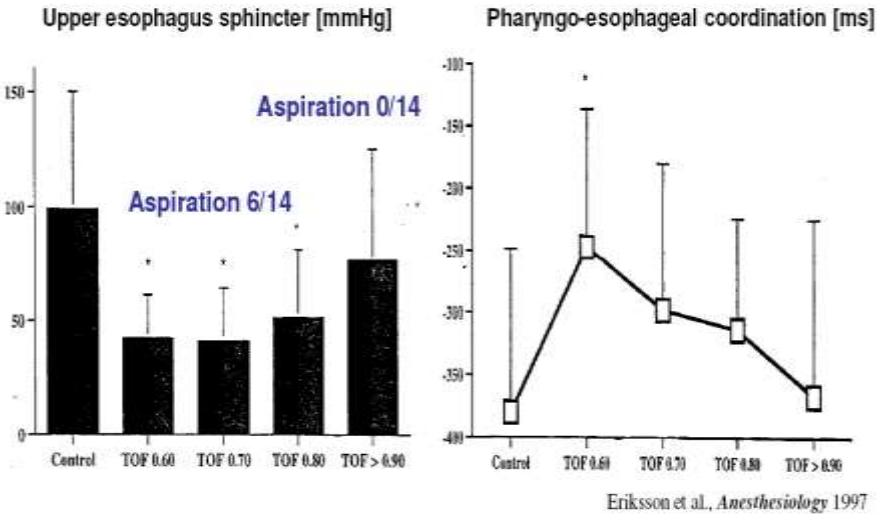
Residual curarizzation was defined on a TOF ratios basis < 0,7. This value is now considered too low since numerous clinical effect of residual blockade have been observed with a TOF ratio between 0.7 and 0.9.

Actually a TOF ratio of 0,9 is considered as a new standard for an adequate recovery of neuromuscolar function.

*Murphy GS. *Minerva Anestesiol*. 2006;72:97-109.
Murphy GS, Szokol JW. *Int Anesthesiol Clin*. 2004;42:25-40.



Frequenza di paralisi residua, in relazione al ritardo tra l'ultima somministrazione di curaro e l'arrivo in PACU.
n = numero di pazienti



Eriksson et al., *Anesthesiology* 1997

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

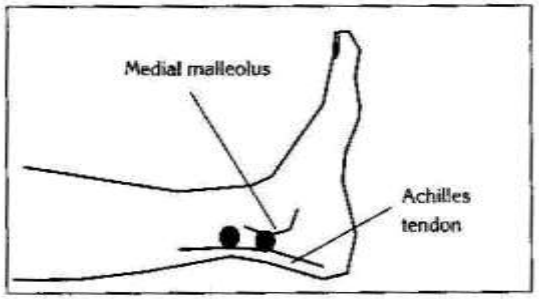
Anaesthesia, 2009, 64 (Suppl. 1), pages 82–89

Monitoring neuromuscular block: an update

T. Fuchs-Buder,[1] J.-U. Schreiber[2] and C. Meistelman[3]

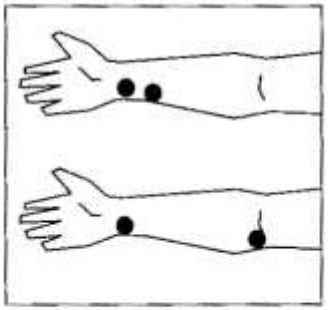
1 Staff, Department of Anaesthesia and Critical Care, Centre Hospitalier Universitaire, Nancy Brabois, France
2 Staff, Department of Anaesthesia, Maastrich UMC, The Netherlands
3 Chairman, Department of Anaesthesia and Critical Care, Centre Hospitalier Universitaire, Nancy Brabois, France

Posterior tibial nerve



The electrodes for the posterior tibial nerve are placed behind the medial malleolus of the tibia.

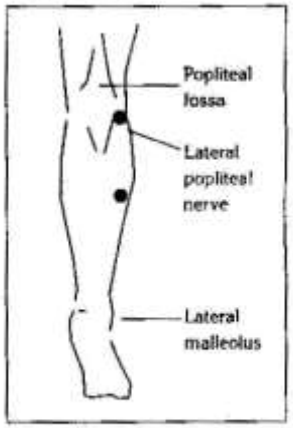
The ulnar nerve



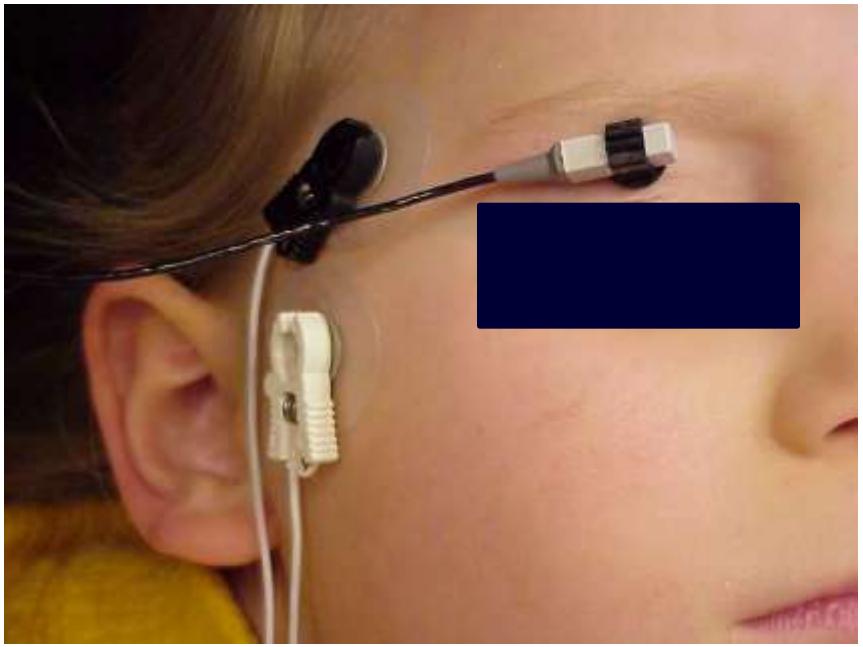
The distal electrode is placed 1-2 cm proximal to the proximal skin crease, centered on the radial side of the tendon of the flexor carpi ulnaris muscle as identified by its insertion into the pisiform bone.

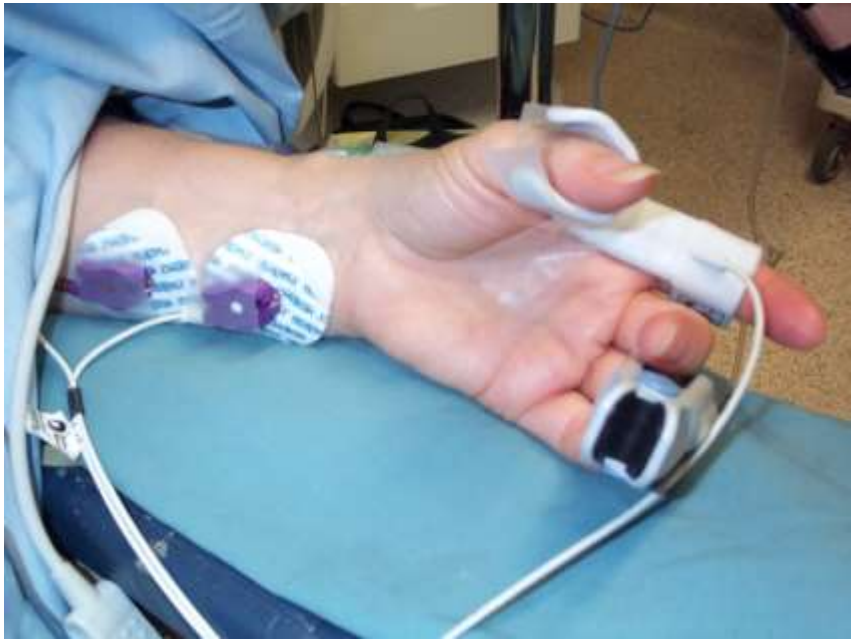
The proximal electrode is placed along the line of the ulnar nerve or over the olecranon.

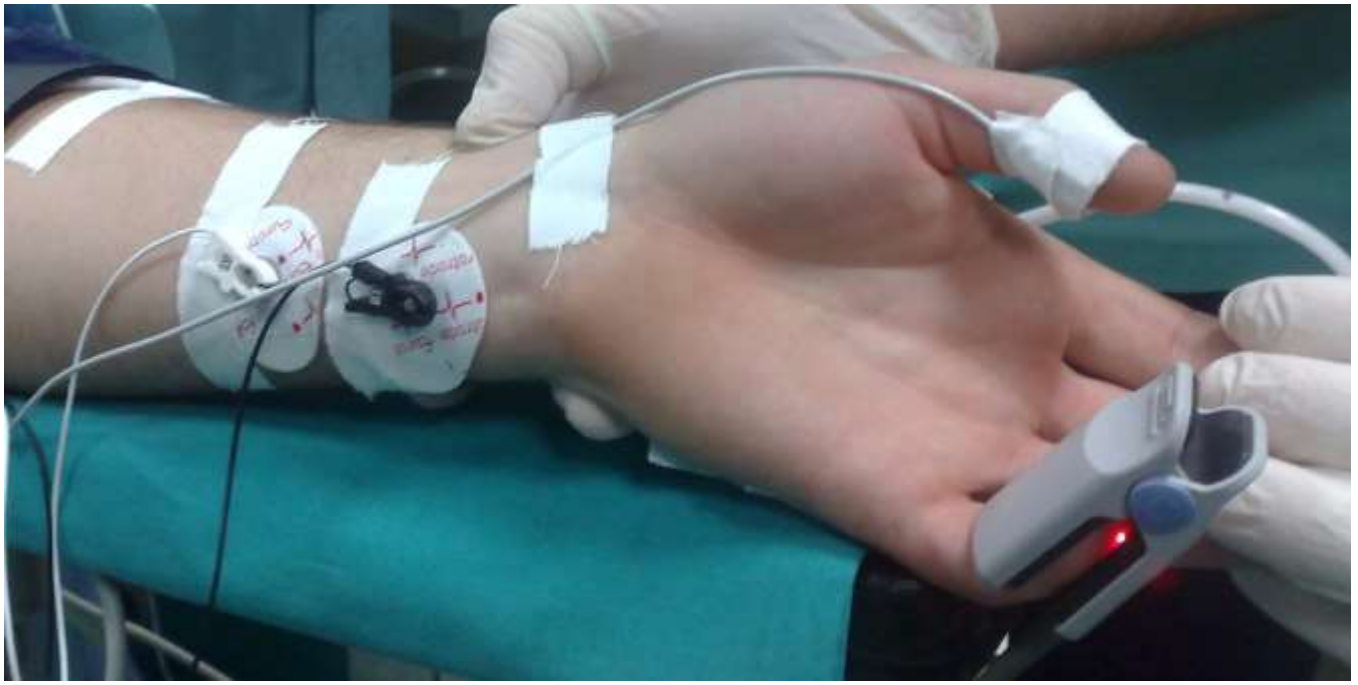
Popliteal nerve



The electrodes for the popliteal nerve are placed lateral to the neck of the fibula.

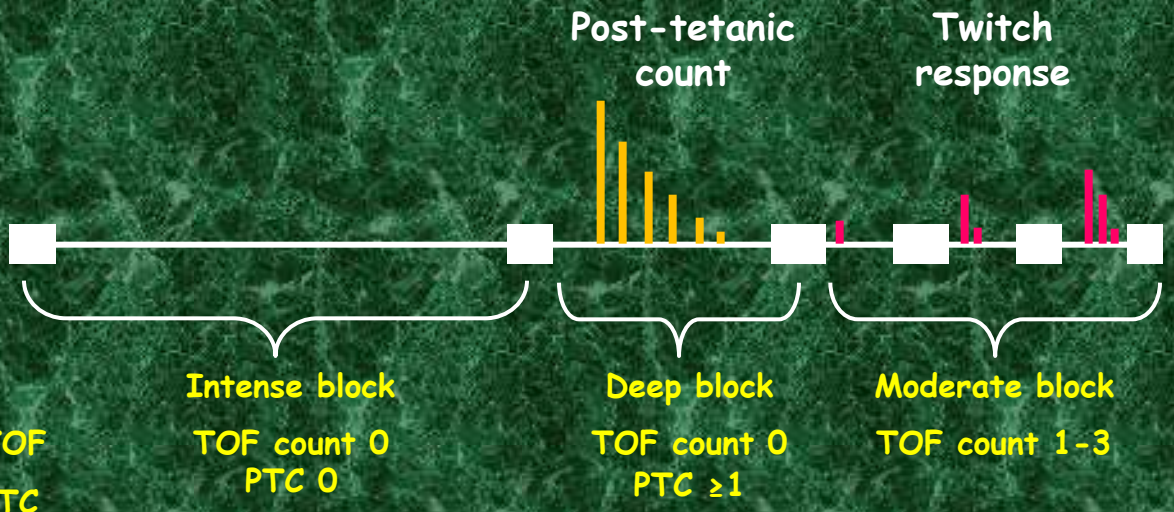






Tipo	frequenza	durata	intervallo	ripetibilità	applicazioni
ST	1 Hz	0,2 ms	1-10 sec		Induzione anestesia
TET	50 Hz	5 sec		> 6min	
TOF	2 Hz	2 sec	0,5 sec	10 sec	Induz. Mant. Estub. Recovery, ICU.
PTC	50 Hz	5 sec		> 6 min	Blocco profondo
DBS	50 Hz	20 ms ciascuno	750ms	> 6 min	

Intensity of blockade

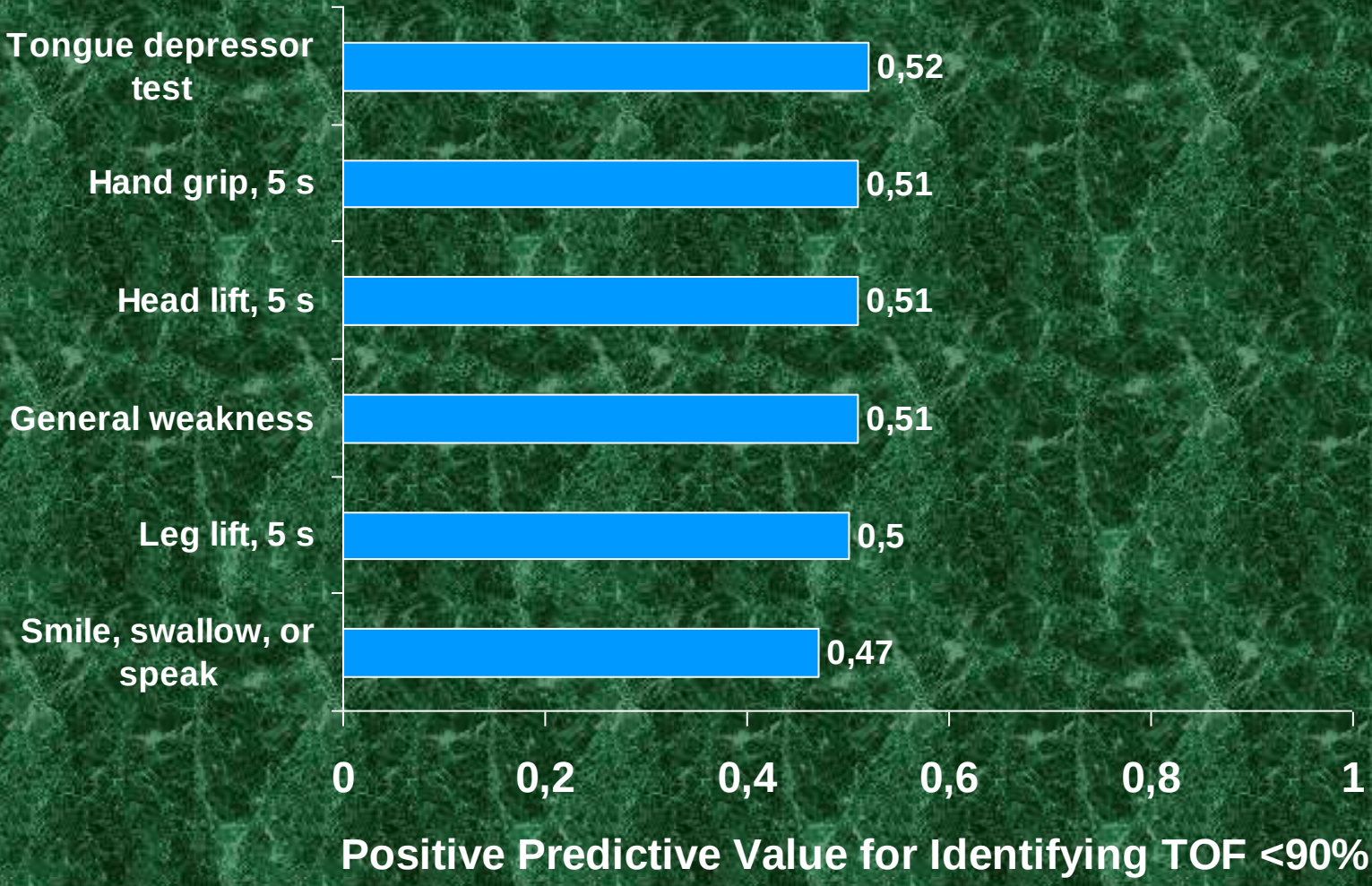


- Intense block : no response to TOF or PTC stimulation
- Deep block : response to PTC but not to TOF stimulation
- Moderate block : return of TOF response

PTC, post-tetanic count; TOF, train-of-four.

Fuchs-Buder T et al. *Acta Anaesthesiol Scand.* 2007;51:789-808.

Clinical tests cannot replace an instrumental monitoring



Cammu G et al. *Anesth Analg.* 2006;102:426-429.

Clinical signs of residual curarization

- Moderate Hypoxaemia : 90% < SpO2 < 93% not improving after active interventions (⬆ O2 flow > 3 l./min. , request to breath deeply, tactile stimulation)

- Severe Hypoxaemia : SpO2 < 90% not improving after active interventions (⬆ O2 flow > 3 l./min. , request to breath deeply, tactile stimulation))

- Respiratory distress signs o ingravescent respiratory failure (respiratory rate > 20 / min. , activation of supplementary muscles, tracheal stridor)

- Inhability to breath deeply when requested

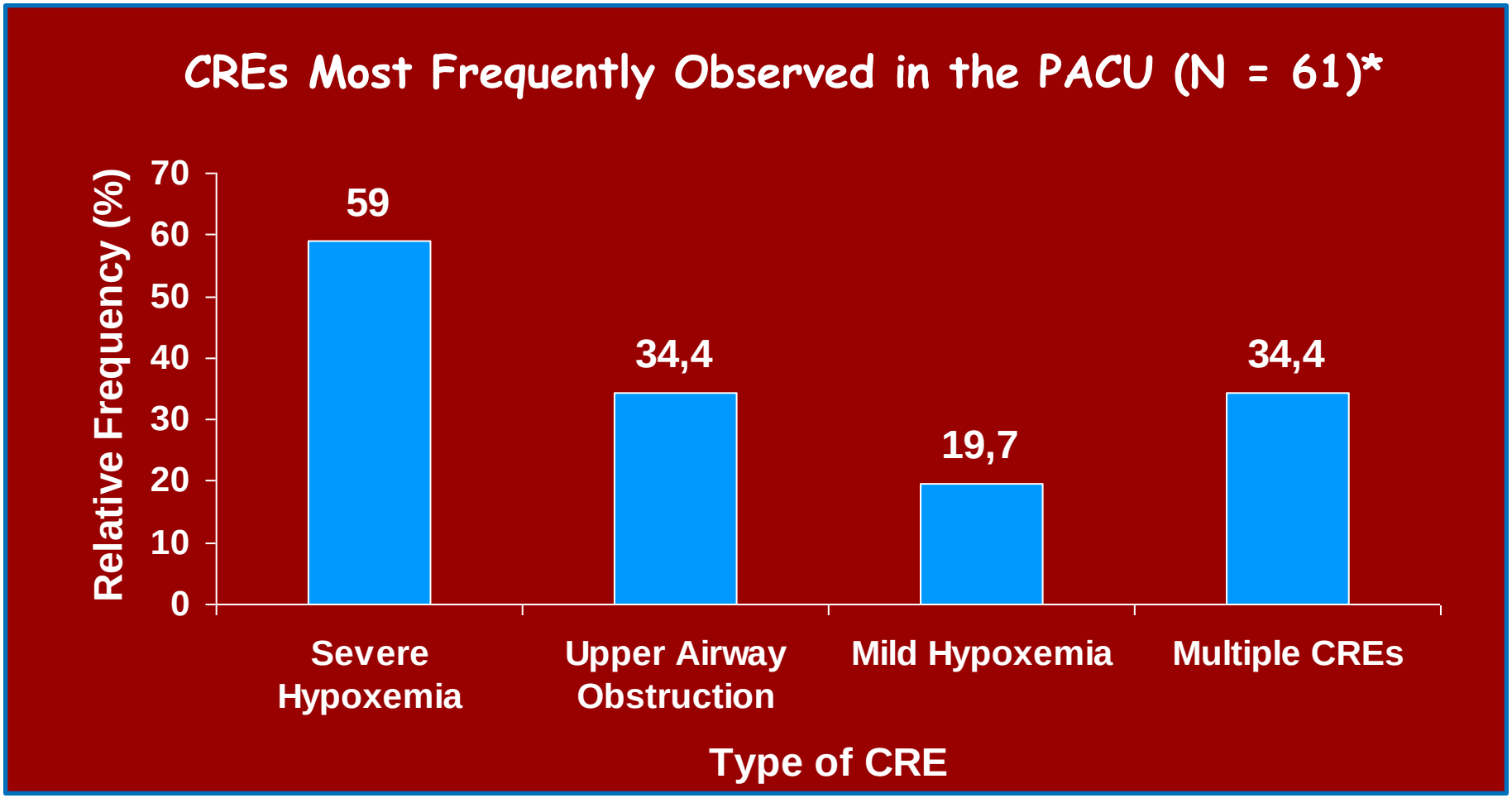
- The patient reports weakness of respiratory muscles or upper airways (difficulty of ventilation, swallowing or languages)

- Patient requires intubation in PACU

- Clinical evidence of post tracheal estubation aspiration syndrome (gastric content observed in the oropharynx associated to hypoxaemia)

Murphy GS et al. *Anesth Analg*. 2008;107:130-137.

"Critical Respiratory Events" (CRE) associated to a residual neuromuscolar blockade



*N = 61 represents the entire cohort of patients who experienced CREs. Only 42 of these patients were able to be matched with a control.
CRE, critical respiratory event; PACU, postanesthesia care unit.

Murphy GS et al. *Anesth Analg.* 2008;107:130-137.

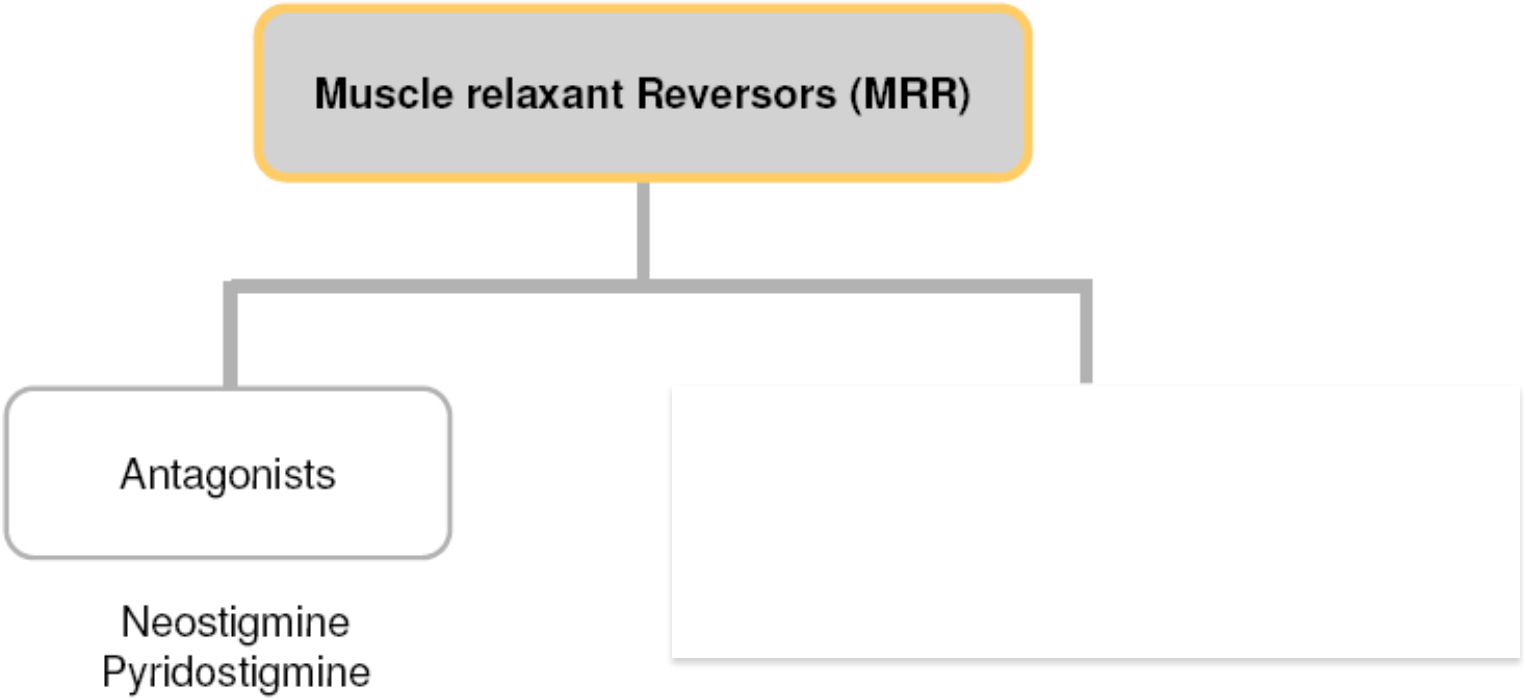

WHICH REVERSAL ?????

The "ideal" reversal agent should…

- Allow a rapid and complete reversal from any kind of block (mild to deep)
- Have a direct activity
- Be a valid alternative to succinilcholine in terms of speed of action and duration
- Not have clinically relevant side effects

Lily P.H. Yang and Susan J. Keam Adis. Drugs 2009;69
K. Jones, M.D.,J.E. Caldwell Anestesiology 2008;109:816-24

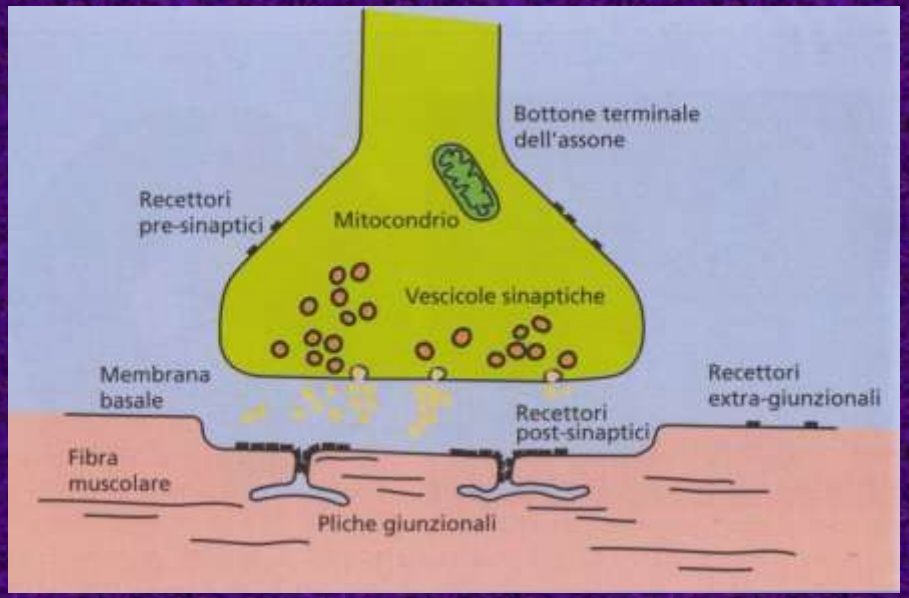
CLASSIFICATION



Fuchs - Buder T et al., Anesth 2007

ANTAGONISTS

- Cholinesterase inhibitors act indirectly by inactivating the enzyme acetylcholinesterase (AChE) in the synaptic cleft of the neuro-muscolar junction (NMJ)
- Acetylcholine (Ach) concentrations increase drammatically, competing with NMBA molecules at the post-synaptic nicotinic receptors.
- Acetylcholinesterase activity gradually returns to normal as the concentration of the cholinesterase inhibitor in the plasma and thus at the NMJ decreases as a result of redistribution, metabolism and escretion.



Limitations of Cholinesterase Inhibitors

- **Relatively slow in reversing neuromuscular blockade**
- **Limited ability to reverse deep blockade**
- **Efficacy influenced by maintenance anesthetics**
- **Well-known side effect profile**
- **Require concomitant administration of anticholinergics**

Bartkowski RR. *Anesth Analg*. 1987;66:594-598.
Kim KS et al. *Anesth Analg*. 2004;99:1080-1085.
Kopman AF et al. *J Clin Anesth*. 2005;17:30-35.

Anticholinesterase side - effects

The increase in Ach concentration induced by an anticholinesterase is not limited to the NMJ, but also occurs at muscarinic sites where Ach is the neurotransmitter.

Muscarinic side-effects include:

- Nausea & vomiting

Anesthesiology
77:162–184, 1992

Postoperative Nausea and Vomiting

Its Etiology, Treatment, and Prevention

Mehernoor F. Watcha, M.D., Paul F. White, Ph.D., M.D., F.F.A.R.A.C.S.†*

The Effects of Antagonizing Residual Neuromuscular Blockade by Neostigmine and Glycopyrrolate on Nausea and Vomiting After Ambulatory Surgery

Girish P. Joshi, MB, BS, MD, FFARCSI, Sandeep A. Garg, MB BS, Amaha Hailey, MD, and Song Y. Yu, MD

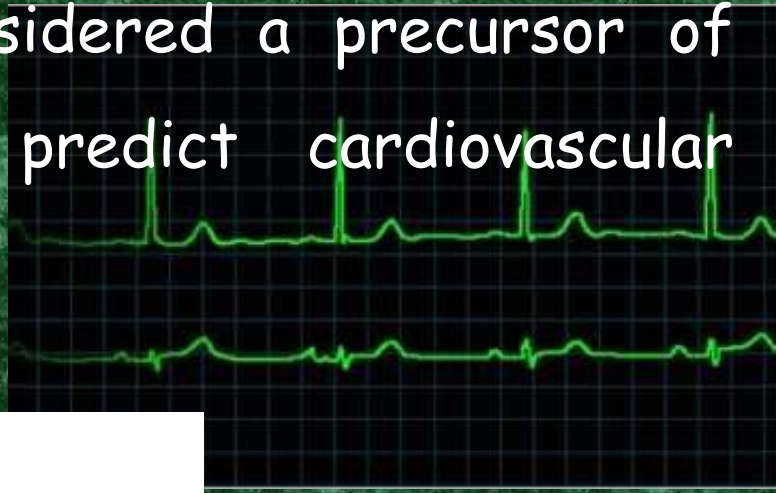
Department of Anesthesiology and Pain Management, University of Texas, Southwestern Medical Center at Dallas, Dallas, Texas

(Anesth Analg 1999;89:628–31)

Anticholinesterase side - effects

- Bradycardia & Q-Tc prolongation

Drug induced Q-Tc interval prolongation may precipitate life - threatening arrhythmias, is considered a precursor of torsades de pointes and may predict cardiovascular complications.



Ventricular fibrillation related to reversal of the neuromuscular blockade in a patient with long QT syndrome

H. PLEYM[1], J. BATHEN[2], O. SPIGSET[3] an
[1]*Department of Anesthesia,* [2]*Department of Inte*
Trondheim, Norway

British Journal of Anaesthesia **103 (1):** 115–29 (2009)
doi:10.1093/bja/aep093 Advance Access publication May 24, 2009

BJA

Reversal of neuromuscular block

A. Srivastava* and J. M. Hunter†

University of Liverpool Critical Care Research Unit, School of Clinical Science, Duncan Building Daulby Street, Liverpool L69 3GA, UK

Anticholinesterase side - effects

- Bronchoconstriction

Cholinergic stimulation produce bronchocostriction, and anticholinesterase have the potential to increase airway resistance.

Neostigmine stimulates the phosphatidylinositol response and thus causes bronchoconstriction.

British Journal of Anaesthesia 101 (3): 344–9 (2008)
doi:10.1093/bja/aen176 Advance Access publication June 16, 2008

BJA

Neostigmine but not sugammadex impairs upper airway dilator muscle activity and breathing

M. Eikermann[1 2 3]

Anticholinesterase Drugs Stimulate Phosphatidylinositol Response in Rat Tracheal Slices

Osamu Shibata, MD, Masahiro Kanairo, MD, Shiping Zhang, MD, Hiroshi Hasuo, MD, Hiroaki Morooka, MD, Toru Fujie, MD, and Koji Sumikawa, MD

Department of Anesthesiology, Nagasaki University School of Medicine, Nagasaki, Japan

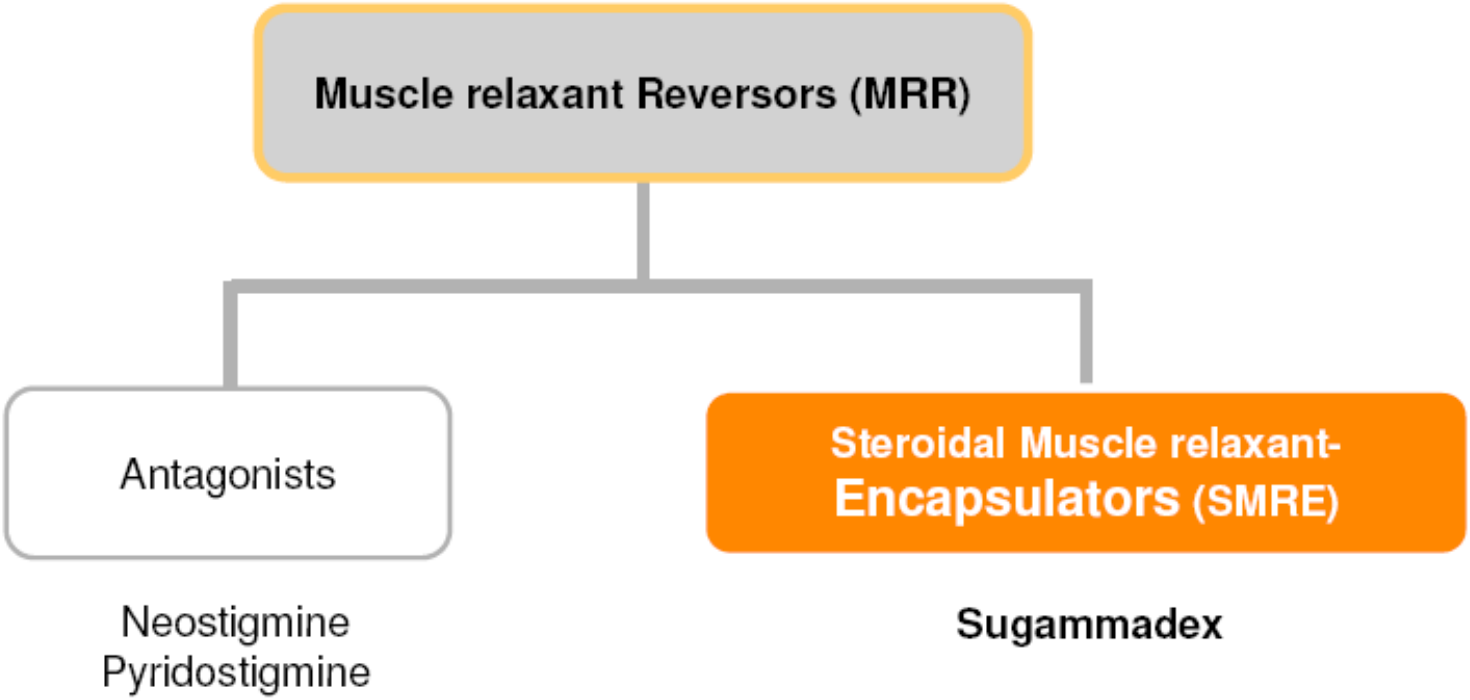
Side Effects Associated With Current Reversal Agents

- ChE inhibitors in the reversal of neuromuscular block can cause
  - Bradycardia
  - Hypersalivation
  - Bronchospasm
  - Increased bronchial secretions
  - Urinary frequency
  - Nausea and vomiting

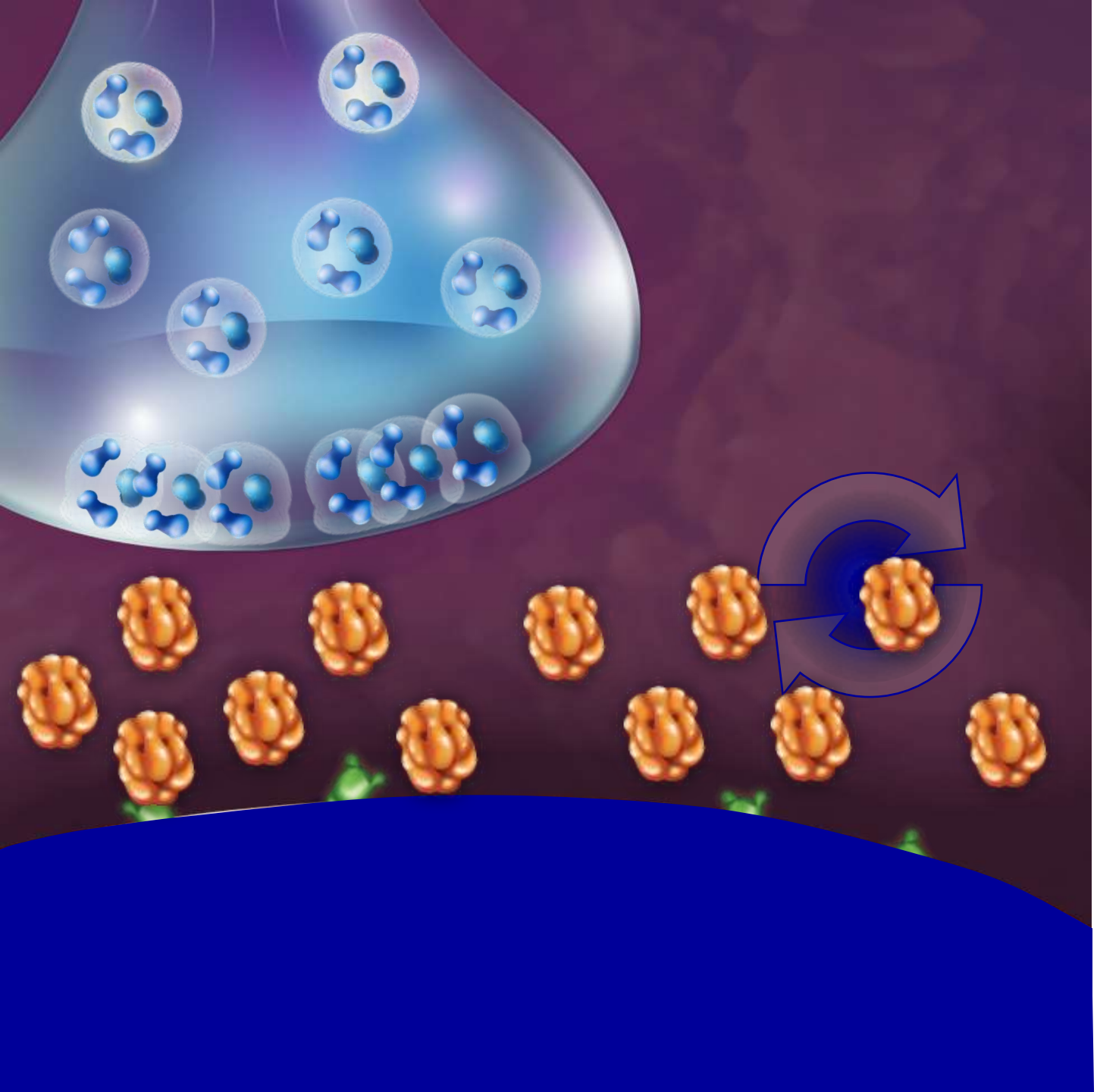
- Coadministration of antimuscarinic agents aids in preventing cholinergic effects but may result in*
  - Tachycardia
  - Dryness of mouth and nose
  - Mydriasis
  - Urinary retention
  - Hypothermia

*Atropine use causes dose-dependent adverse effects.
ChE, cholinesterase.

CLASSIFICATION



Fuchs - Buder T et al., Anesth 2007

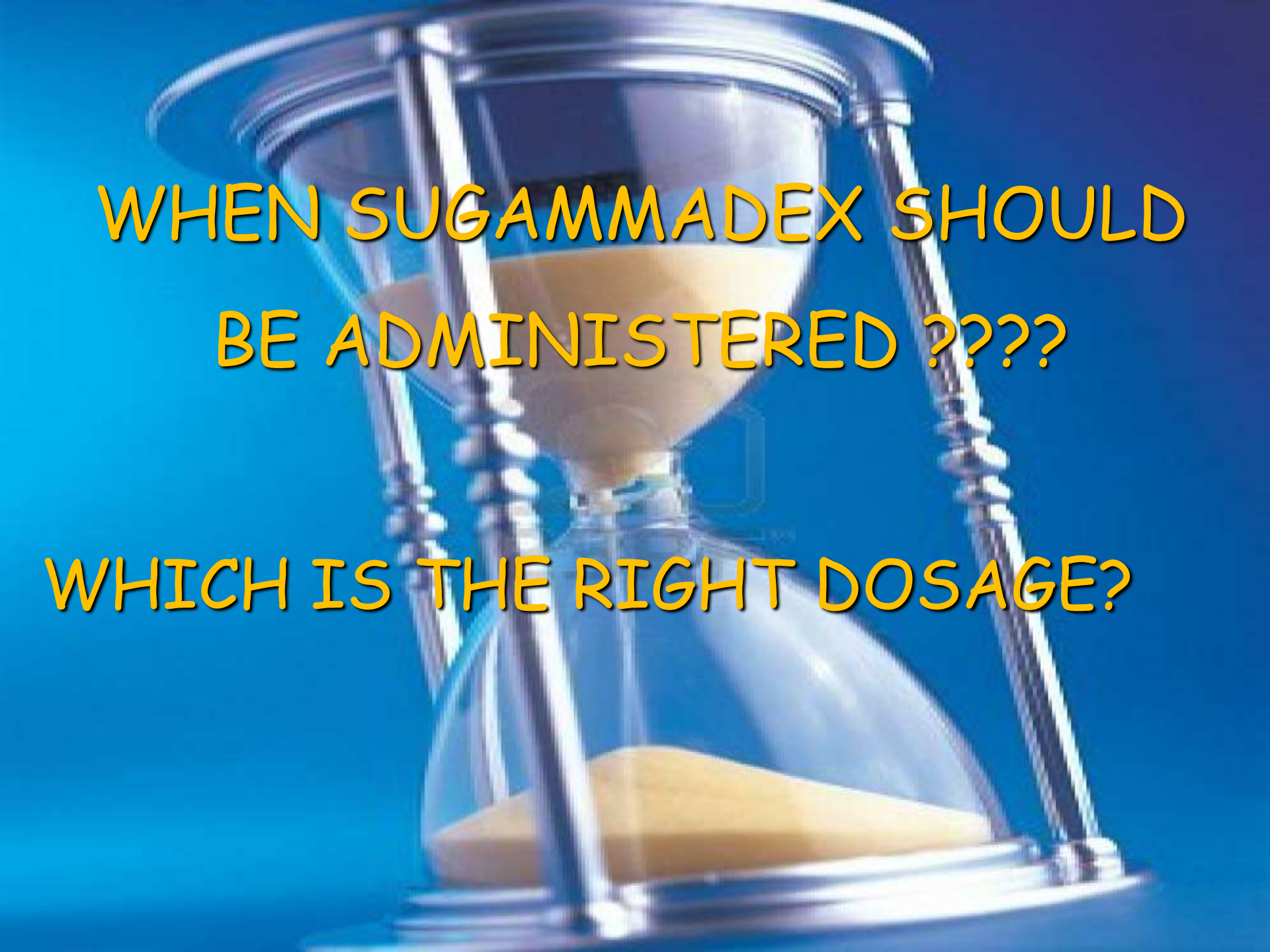


Acetylcholine

Cholinesterase

Rocuronium

Sugammadex


WHEN SUGAMMADEX SHOULD BE ADMINISTERED ????
WHICH IS THE RIGHT DOSAGE?

Sugammadex, a Selective Reversal Medication for Preventing Postoperative Residual Neuromuscular Blockade

Amir Abrishami, Joyce Ho, Jean Wong, Ling Yin, Frances Chung

BACKGROUND: Sugammadex is the first selective relaxant binding agent that has been studied for reversal of neuromuscular blockade induced by rocuronium and other steroidal non-depolarizing neuromuscular blocking agents (NMBAs).

OBJECTIVES: To assess the efficacy and safety of sugammadex in reversing neuromuscular blockade induced by steroidal non-depolarizing NMBAs and in preventing postoperative residual neuromuscular blockade.

SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2008, Issue 3), MEDLINE (1950 to August 2008), and EMBASE (1980 to August 2008). In addition, we handsearched reference lists of relevant articles and meeting abstracts. Furthermore, we contacted the medication's manufacturer for more information.

SELECTION CRITERIA: All randomized controlled trials (RCTs) on adult patients (≥ 18 years old) in which sugammadex was compared with placebo or other medications, or in which different doses of sugammadex were compared with each other. We excluded non-randomized trials and studies on healthy volunteers.

DATA COLLECTION AND ANALYSIS: We independently performed determination of trial inclusion, quality assessment, and data extraction. We applied standard meta- analytic techniques.

MAIN RESULTS: We included18 RCTs (n = 1321 patients). Seven trials were published as full-text papers, and 11 trials only as meeting abstracts. All the included trials had adequate methods of randomization and allocation concealment. The results suggest that, compared with placebo or neostigmine, sugammadex can more rapidly reverse rocuronium-induced neuromuscular blockade regardless of the depth of the block. We identified 2, 4, and 16 mg/kg of sugammadex for reversal of rocuronium-induced neuromuscular blockade at T2 reappearance , 1 to 2 post-tetanic counts, and 3 to 5 minutes after rocuronium, respectively. The number of trials are very limited regarding vecuronium and pancuronium. Serious adverse events occurred in < 1% of all patients who received the medication. There was no significant difference between sugammadex and placebo in terms of the prevalence of drug-related adverse events (RR 1.20, 95% CI 0.61 to 2.37; P = 0.59, I2 = 0%, 5 RCTs). Also, no significant difference was found between sugammadex and neostigmine for adverse events (RR 0.98, 95% CI 0.48 to1.98; P = 0.95, I2 = 43%, 3 RCTs).

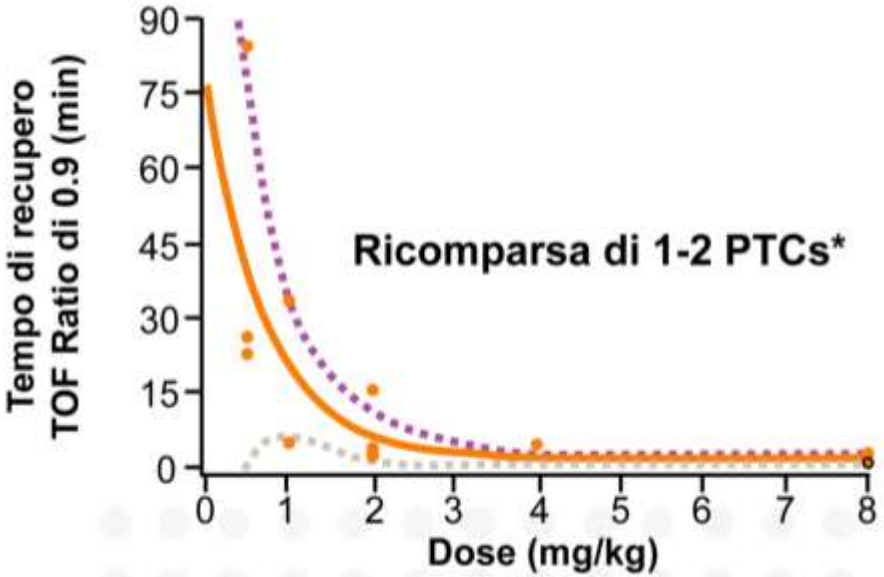
AUTHORS' CONCLUSIONS: Sugammadex was shown to be effective in reversing rocuronium-induced neuromuscular blockade. This review has found no evidence of a difference in the instance of unwanted effects between sugammadex, placebo or neostigmine. These results need to be confirmed by future trials on larger patient populations and with more focus on patient-related outcomes.

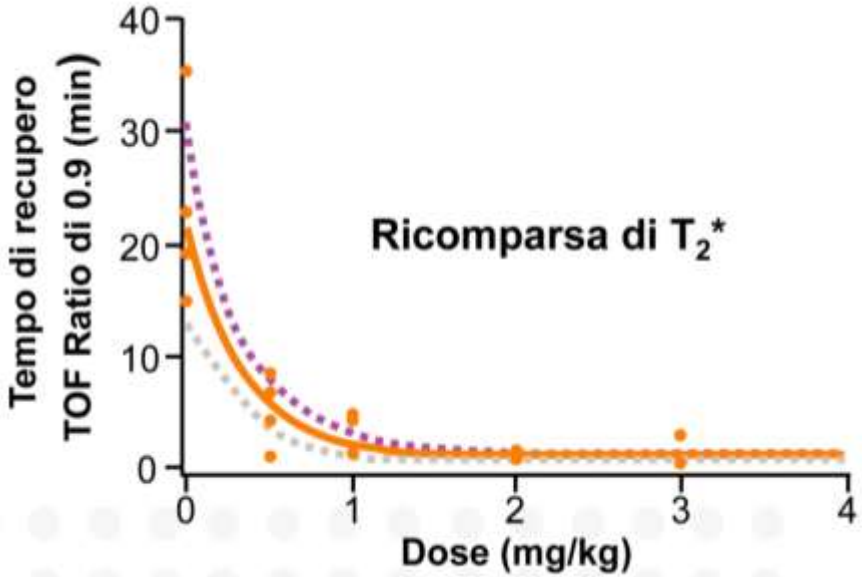
Abrishami A, Ho J, Wong J, Yin L, Chung F. Sugammadex, a selective reversal medication for preventing postoperative residual neuromuscular blockade. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD007362. DOI: 10.1002/14651858.CD007362.pub2.

Sugammadex: dose-response ratio

- Real time with TOF 0.9

Expected time with TOF 0.9





When dosage is increased, Sugammadex allows a rapid recovery even from higher levels of neuromuscolare blockade

**Neuromuscolar blockade induced by Rocuronium 0.6 mg/kg.*
PTC, post tetanic count

Sorgenfrei IF et al. Anesthesiology. 2006;104:667-674
Groudine SB et al. Anesth Analg. 2007;104:555-562

Sugammadex at Re-appearance of T2 after 0.6 mg/kg Roc

summarized data of all studies

	Plazebo	0,5 mg/kg	1,0 mg/kg	2,0 mg/kg	3,0 mg/kg	4,0 mg/kg	6,0 mg/kg
N	25	35	38	38	8	39	4
Mean (SD)							
Media							
Min-M							

Sugammadex at 1-2 PTC after 0.6 mg/kg Roc

summarized data of all studies

	placebo	0,5 mg/kg	1,0 mg/kg	2,0 mg/kg	4,0 mg/kg	6,0 mg/kg	8,0 mg/kg
N	3	18	27	34	31	6	34
Mean (SD)	35.6 (9.0)						
Median	30.6						
Min-Max	30.1-46						

Time to TOF 0.9 after 16 mg/kg Sugammadex

3 min. after 1.2 mg/kg Rocuronium

	Rocuronium + sugammadex	Rocuronium + Placebo
N	65	5
Mean (SD)	1.7	134.4
95% CI	1.4-1.9	92.6-195.6
Median	1.5	129.7
Min-Max	0.5-14.3	87.3-209.1

British Journal of Anaesthesia **100** (5): 622–30 (2008)
doi:10.1093/bja/aen037 Advance Access publication April 2, 2008

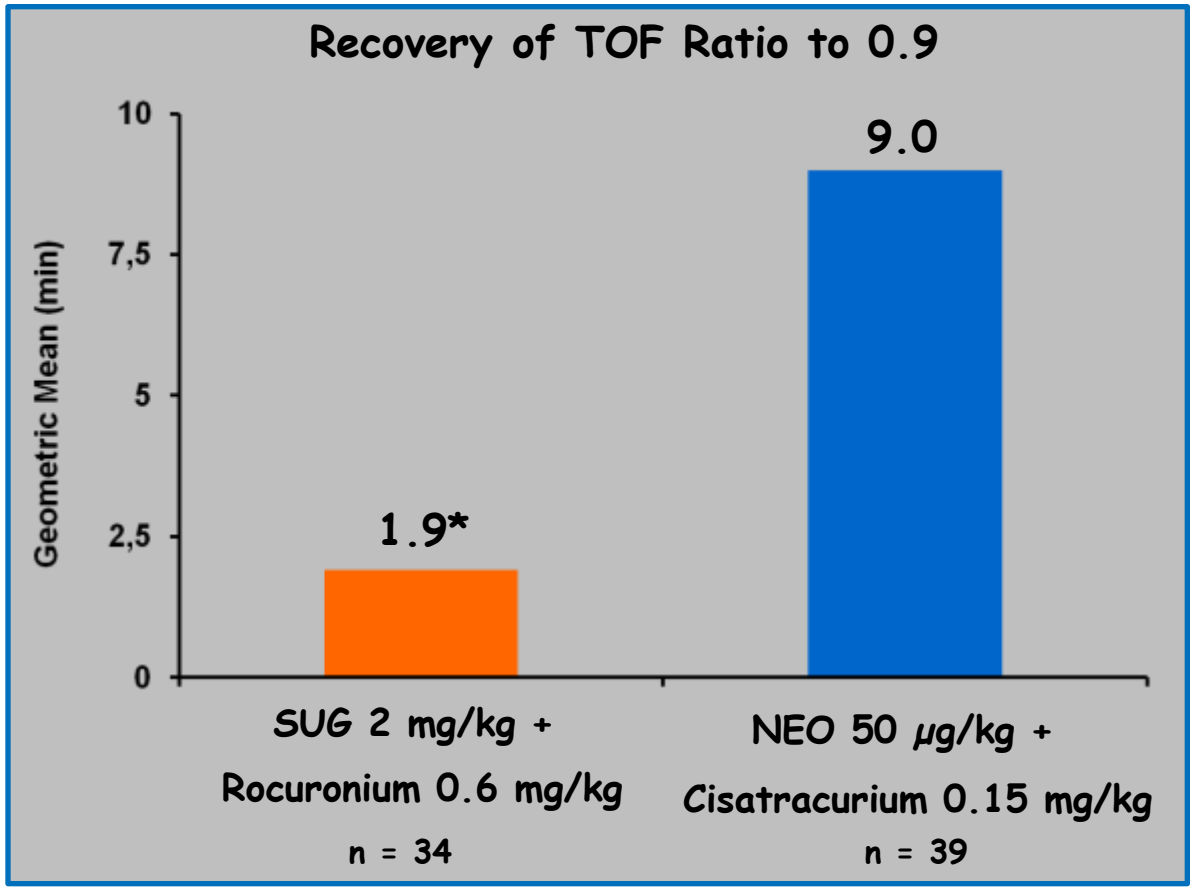
BJA

CLINICAL PRACTICE

Reversal of rocuronium-induced neuromuscular block with sugammadex is faster than reversal of cisatracurium-induced block with neostigmine

E. A. Flockton[1]*, P. Mastronardi[2], J. M. Hunter[1], C. Gomar[3], R. K. Mirakhur[4†], L. Aguilera[5], F. G. Giunta[6], C. Meistelman[7] and M. E. Prins[8†]

	Rocuronium–sugammadex ($n=34$)	Cisatracurium–neostigmine ($n=39$)	*P*-value
Recovery of TOF ratio to 0.7			
n	32	36	
Geometric mean	1.4	5.1	<0.0001*
Median (range)	1.2 (0.7–2.9)	4.7 (2.4–10.9)	
Recovery of TOF ratio to 0.8			
n	32	36	
Geometric mean	1.6	6.5	<0.0001*
Median (range)	1.5 (0.7–3.4)	5.9 (3.2–15.6)	
Recovery of TOF ratio to 0.9			
n	32	34	
Geometric mean	1.9	9.0	<0.0001*
Median (range)	1.9 (0.7–6.4)	7.3 (4.2–28.2)	

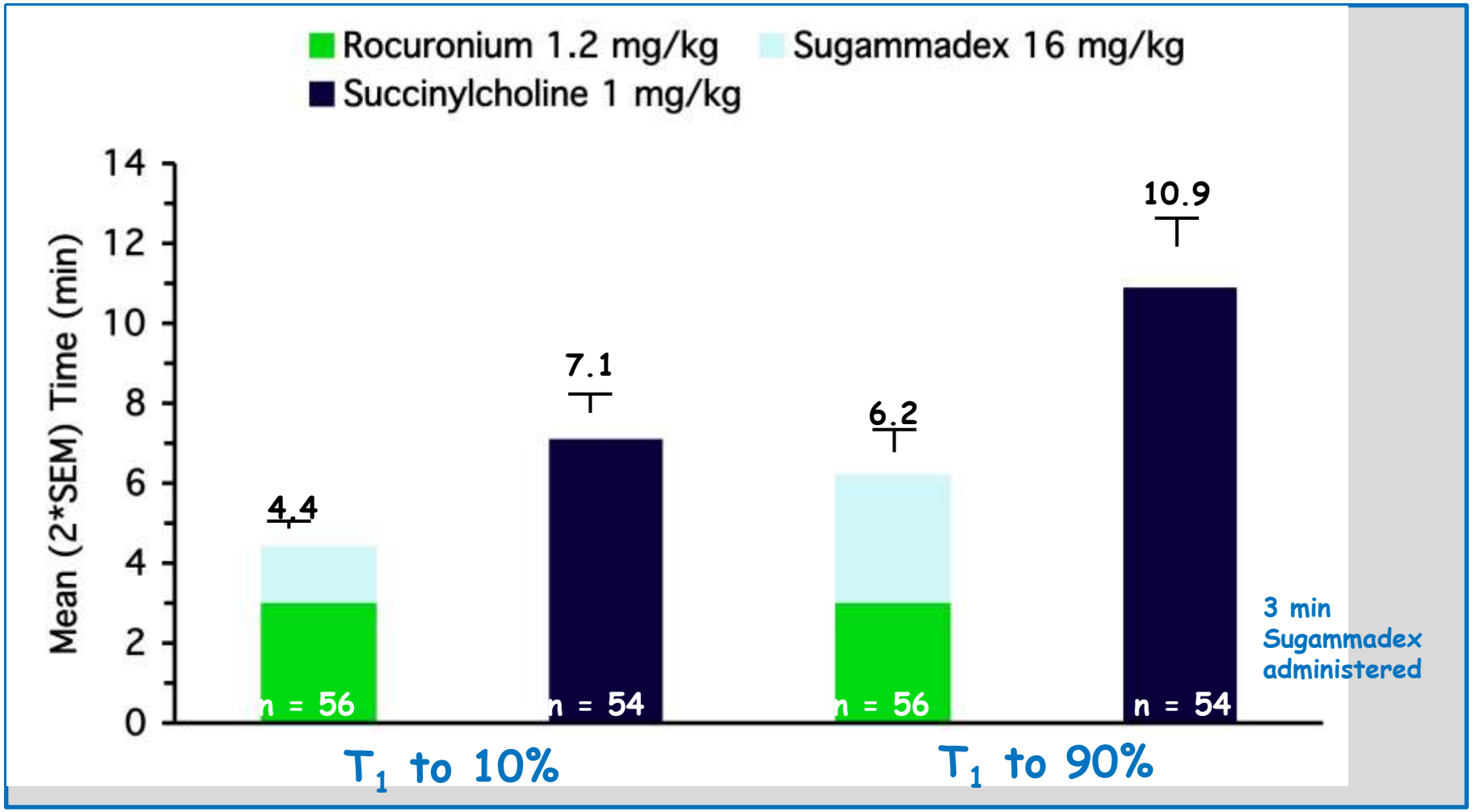


Anesthesiology 2009; 110:1020–5

Reversal of Profound Neuromuscular Block by Sugammadex Administered Three Minutes after Rocuronium

A Comparison with Spontaneous Recovery from Succinylcholine

Chingmuh Lee, M.D.,* Jonathan S. Jahr, M.D.,† Keith A. Candiotti, M.D.,‡ Brian Werriner, M.D.,§ Mark H. Zornow, M.D.,|| Mohamed Naguib, M.D.#



Sugammadex in the airway managment

Br J Anaesth. 2012 Apr;108(4):682-9. doi: 10.1093/bja/aer503. Epub 2012 Feb 6.

Rapid sequence induction and intubation with rocuronium-sugammadex compared with succinylcholine: a randomized trial.

Sørensen MK[1], Bretlau C, Gätke MR, Sørensen AM, Rasmussen LS.

RSII with rocuronium followed by sugammadex allowed earlier re-establishment of spontaneous ventilation than with succinylcholine.

SAFETY PROFILE

Reversal of Rocuronium-Induced Neuromuscular Block with the Novel Drug Sugammadex Is Equally Effective Under Maintenance Anesthesia with Propofol or Sevoflurane

Bernard F. Vanacker, MD, PhD*
Karel M. Vermeyen, MD, PhD†
Michel M. R. F. Struys, MD, PhD‡
Henk Rietbergen, MSc§
Eugene Vandermeersch, MD, PhD*
Vera Saldien, MD†
Alain F. Kalmar, MD‡
Martine E. Prins, MSc§

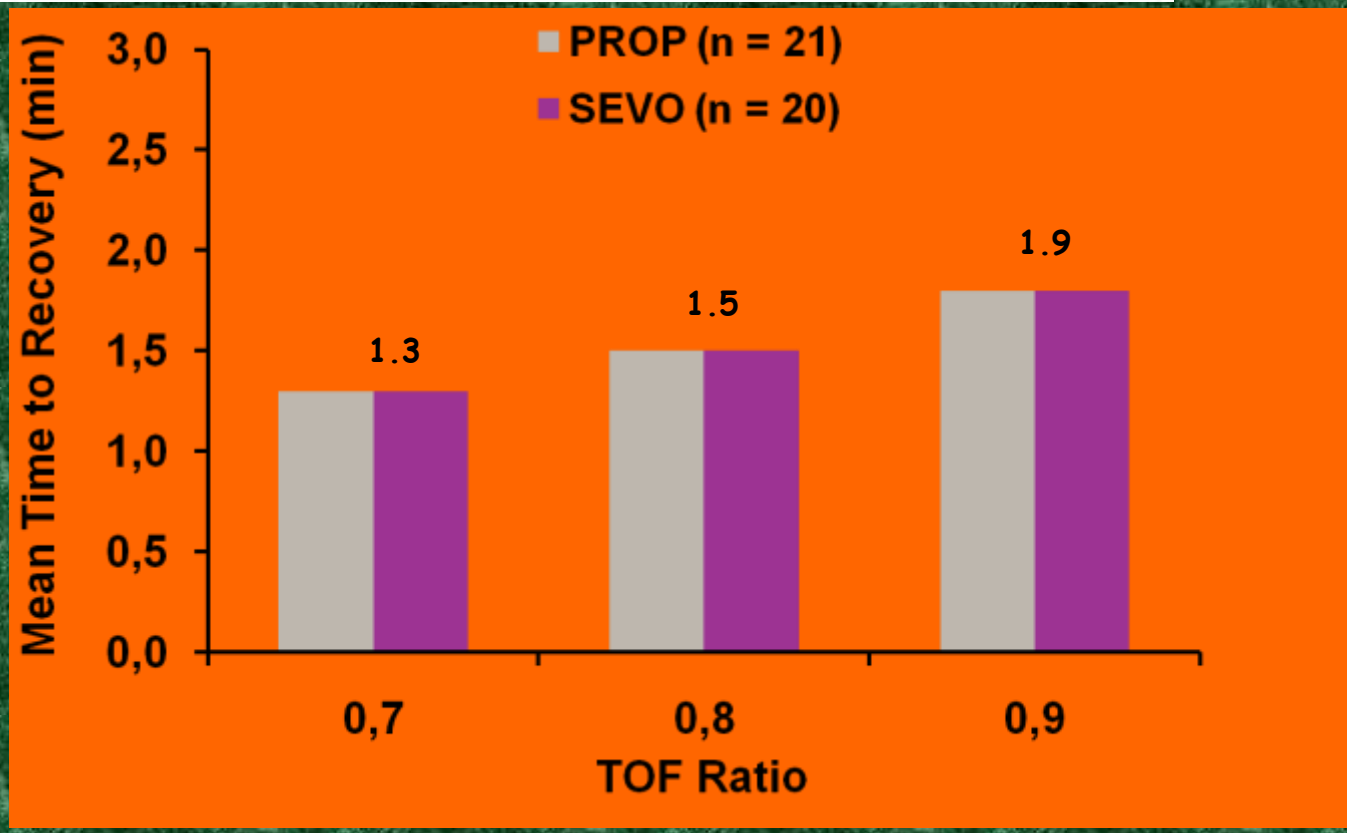
In this study we investigated whether the novel reversal drug, sugammadex, is equally effective at reversing rocuronium-induced neuromuscular block (NMB) in patients under propofol or sevoflurane maintenance anesthesia. After receiving propofol for induction, patients were randomized to propofol (n = 21) or sevoflurane (n = 21). Rocuronium 0.6 mg/kg was administered for tracheal intubation. NMB was monitored using acceleromyography. At reappearance of the second twitch of the train-of-four ratio, sugammadex 2.0 mg/kg was administered by IV bolus. The primary end-point was time from start of sugammadex administration to recovery of train-of-four ratio to 0.9. Mean recovery time was 1.8 min after both propofol and sevoflurane anesthesia. The 95% confidence interval for the difference in recovery time between the 2 groups (−0.5 to +0.4 min) was well within the predefined equivalence interval (−1 to +1 min), indicating that recovery from NMB was unaffected by maintenance anesthesia. Thirteen patients (propofol n = 4; sevoflurane n = 9) experienced adverse events; these were treatment-related in 4 patients (propofol n = 3; sevoflurane n = 1). There were no treatment-related serious adverse events and no discontinuations or deaths. No residual paralysis occurred. The safety profile of sugammadex was somewhat more favorable under propofol than under sevoflurane anesthesia.

(Anesth Analg 2007;104:563–8)

Table 3. Time (min) From Administration of Sugammadex (2.0 mg/kg) to Recovery of the Train-of-Four (TOF) Ratio (Per Protocol Population)

	Treatment group	
	Propofol (n = 21)	Sevoflurane (n = 20)
Time to recovery of TOF ratio to 0.9	1.8 (0.7) [0.9–3.4]*	1.8 (0.7) [1.1–4.5]
Time to recovery of TOF ratio to 0.8	1.5 (0.5) [0.9–2.9]	1.5 (0.3) [1.1–2.1]
Time to recovery of TOF ratio to 0.7	1.3 (0.5) [0.8–2.4]	1.3 (0.3) [0.7–1.9]

Values are mean (SD) [range]. TOF = train-of-four.
* Data missing for one patient, n = 20.



*Rocuronium 0.6 mg/kg followed by Sugammadex 2 mg/kg.
†Data missing for 1 patient.

Anesthesiology 2009; 110:284–94

Reversal of Rocuronium-induced Neuromuscular Blockade with Sugammadex in Pediatric and Adult Surgical Patients

Benoît Plaud, M.D., Ph.D.,* Olli Meretoja, M.D., Ph.D.,† Rainer Hofmockel, M.D., Ph.D.,‡ Julien Raft, M.D.,§ Peter A. Stoddart, M.R.C.P., F.R.C.A.,|| Jacqueline H. M. van Kuijk, M.Sc.,# Yvonne Hermens, M.Sc.,** Rajinder K. Mirakhur, M.D., Ph.D., F.R.C.A.††

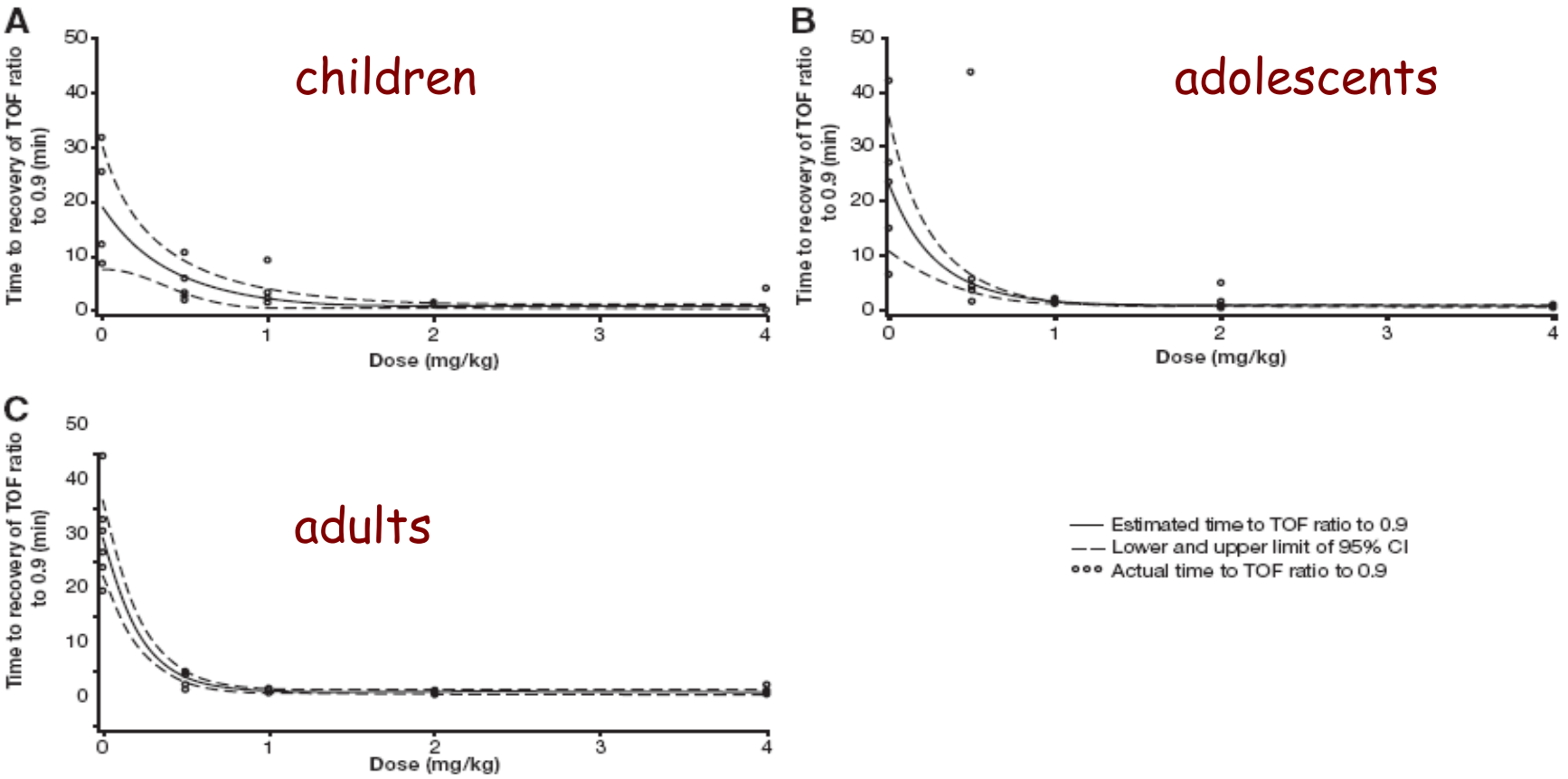


Fig. 1. Estimated dose-response relation between the time from the start of administration of sugammadex/placebo to recovery of the TOF ratio to 0.9 and the dose of sugammadex for (*A*) children (n = 22), (*B*) adolescents (n = 28), and (*C*) adults (n = 26) (per-protocol group). CI = confidence interval; TOF = train-of-four.

Pediatric Anesthesia

Correspondence

Case report: sugammadex used to successfully reverse vecuronium-induced neuromuscular blockade in a 7-month-old infant

Case Report

Sugammadex Use in the Reversal of Deep Neuromuscular Block in a Six-Year-Old Child after an Emergency Procedure in Ear, Nose and Throat Surgery Department

Paolo Murabito, Giovanni Savarino, Caren Conticello, Marco Farina, Carmela Stissi and Marinella Astuto

Department of Anaesthesia and Intensive Care, "Policlinico" University Hospital, Catania, Italy

clearly visualized. There appeared to be a polyp on the lateral wall of the pharynx obscuring the view. An attempt at intubation was unsuccessful.

A return was made to mask ventilation while the fiber-optic scope was prepared. On the first attempt, no view of the larynx could be obtained. On the second attempt, a view of the larynx was obtained but the endotracheal tube could not be passed as it was insufficiently lubricated. The field was noted to be bloody at this stage.

Mask ventilation was becoming more difficult with an extended period of mask ventilation expected. It was now 15 min since induction. A discussion took place about the potential role of sugammadex. It was decided to administer 4 mg·kg^{-1} in the first instance, with the option to increase the dose if required. Twenty-five milligram of sugammadex was administered intravenously, with very

rocuronium.

2.Sugammadex has been used effectively and safely in the infant age group.

3.Sugammadex should be considered when faced with the can't intubate - can't ventilate scenario in the pediatric population.

Efficacy, Safety, and Pharmacokinetics of Sugammadex for the Reversal of Rocuronium-induced Neuromuscular Blockade in Elderly Patients

David L. McDonagh, M.D.,* Patrick E. Benedict, M.D.,† Anthony L. Kovac, M.D.,‡
David R. Drover, M.D.,§ Neil W. Brister, M.D., Ph.D.,|| Jovino B. Morte, M.D.,# Terri G. Monk, M.D., M.S.**

Anesthesiology 2011; 114:318–29

Henry Allingham (6 Jun 1896 - 19 Jun 2011)

Table 2. Time from the Start of Administration of Sugammadex to Recovery of the TOF Ratio to 0.9, 0.8, and 0.7 by Age Group (ITT Population)

Time Variables	Adult Subjects Aged 18–64 yr (n = 48)	Elderly Subjects Aged 65–74 yr (n = 62)	Old-Elderly Subjects Aged 75 yr or Older (n = 40)	Subtotal Aged 65 yr or Older (n = 102)
Time to recovery of the TOF ratio to 0.9 (imputed analysis), No. of subjects	48	62	40	102
Geometric mean (95% CI)	2.3 (2.0–2.6)	2.6 (2.3–2.9)	3.6 (3.1–4.1)	2.9 (2.7–3.2)
Mean (SD)	2.5 (1.4)	2.9 (1.6)	3.9 (1.7)	3.3 (1.7)
Median	2.2	2.6	3.6	2.9
Minimum–maximum	1.2–7.4	0.9–8.8	1.0–9.9	0.9–9.9
P value*				0.022
Time to recovery of the TOF ratio to 0.9 (excluding patients with imputed data), No. of subjects	45	57	35	92
Geometric mean (95% CI)	2.1 (1.9–2.4)	2.4 (2.1–2.7)	3.4 (2.9–3.9)	2.7 (2.5–3.0)
Mean (SD)	2.3 (1.0)	2.7 (1.4)	3.7 (1.6)	3.1 (1.6)
Median	2.1	2.5	3.5	2.8
Minimum–maximum	1.2–6.2	0.9–8.8	1.0–9.9	0.9–9.9
P value*				0.017
Time to recovery of the TOF ratio to 0.8 (imputed analysis), No. of patients	48	62	40	102
Geometric mean (95% CI)	1.9 (1.7–2.1)	2.1 (1.8–2.4)	2.8 (2.4–3.3)	2.3 (2.1–2.6)
Mean (SD)	2.1 (1.0)	2.4 (1.5)	3.1 (1.4)	2.7 (1.5)
Median	1.7	2.0	2.9	2.2
Minimum–maximum	1.1–6.2	0.7–8.8	0.8–6.2	0.7–8.8
P value*				0.035
Time to recovery of the TOF ratio to 0.7 (imputed analysis), No. of patients	48	62	40	102
Geometric mean (95% CI)	1.6 (1.5–1.8)	1.8 (1.6–2.0)	2.4 (2.1–2.8)	2.0 (1.8–2.2)
Mean (SD)	1.8 (0.8)	2.1 (1.5)	2.7 (1.2)	2.3 (1.4)
Median	1.6	1.7	2.4	1.9
Minimum–maximum	0.9–4.9	0.7–8.3	0.8–4.9	0.7–8.3
P value*				0.027

Time data are given in minutes.

* Comparison between the adult group (aged 18–64 yr) and the elderly/old-elderly group combined (65 yr or older).

CI = confidence interval; ITT = intention-to-treat; TOF = train-of-four.

Sugammadex & pulmonary diseases

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2009, **64** (Suppl. 1), pages 55–65

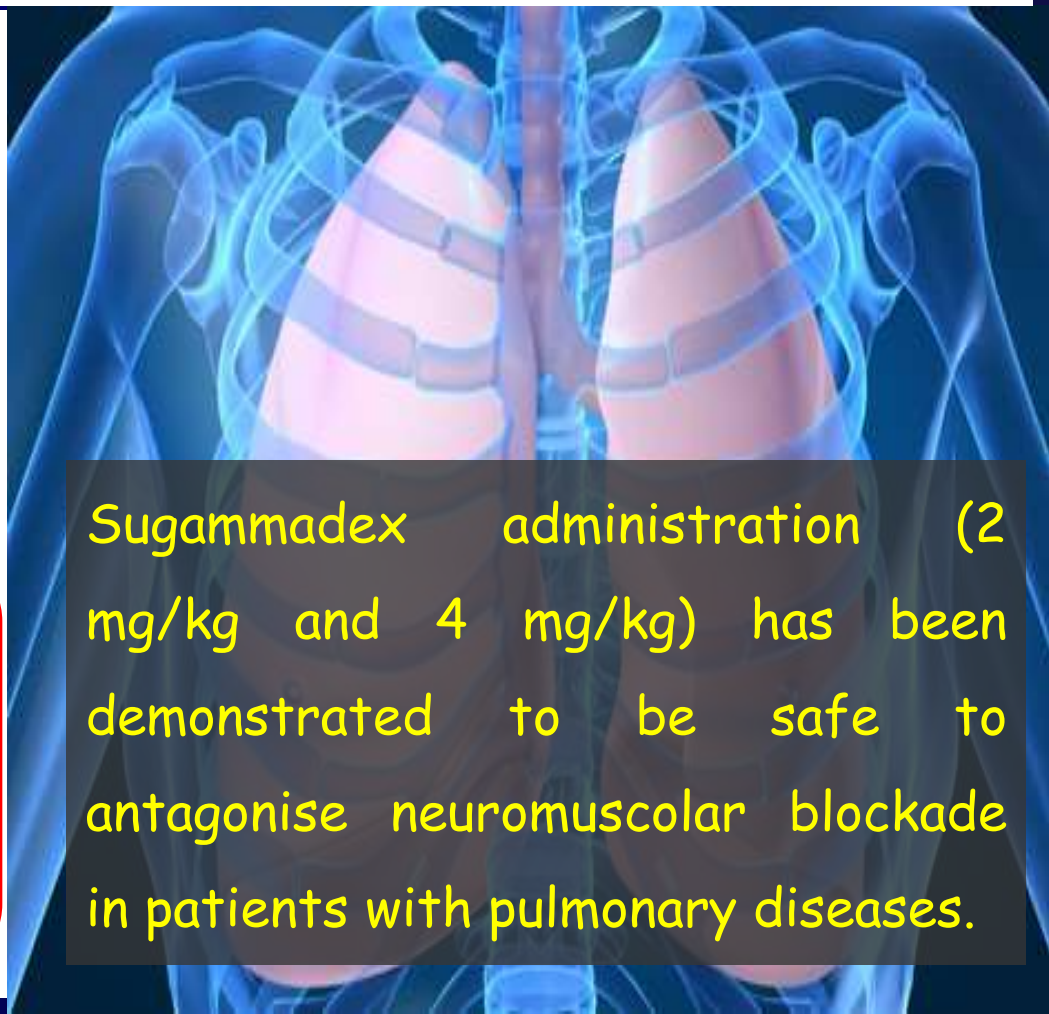
Neuromuscular blocking drugs and their antagonists in patients with organ disease

R. G. Craig[1] and J. M. Hunter[2]

Pulmonary disease

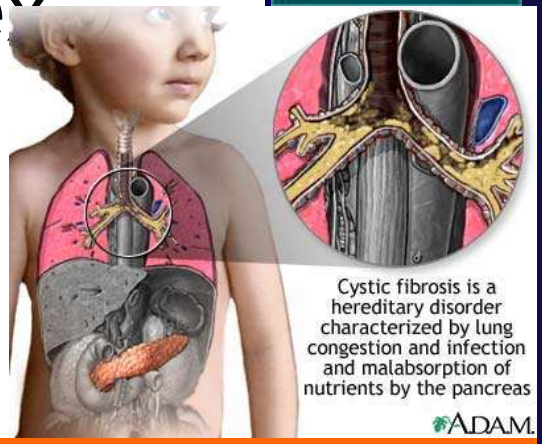
Amao et al. [65] administered sugammadex to reverse rocuronium-induced neuromuscular block in 77 patients with pulmonary disease (ASA physical status 2–3). Thirty-nine patients were given sugammadex 2 $mg.kg^{-1}$ and 38 patients were given sugammadex 4 $mg.kg^{-1}$, administered at the reappearance of T2. The geometric mean time from the start of sugammadex administration to recovery of the TOF ratio to 0.9 was 1.8 min in the sugammadex 4 $mg.kg^{-1}$ group, and 2.1 min in the sugammadex 2 $mg.kg^{-1}$ group.

Of the 77 patients with pulmonary disease who received sugammadex, two developed bronchospasm [65]. These were both asthmatic patients; in one case the bronchospasm occurred 1 min after tracheal extubation and lasted 4 min, and in the other it occurred 55 min after sugammadex. It is possible that bronchospasm in these patients was related to sugammadex administration. There was no evidence of residual neuromuscular block or recurarisation.



Sugammadex administration (2 mg/kg and 4 mg/kg) has been demonstrated to be safe to antagonise neuromuscolar blockade in patients with pulmonary diseases.

The use of rocuronium in a patient with cystic fibrosis and end-stage lung disease made safe by sugammadex reversal



MV Porter, MS Paleologos

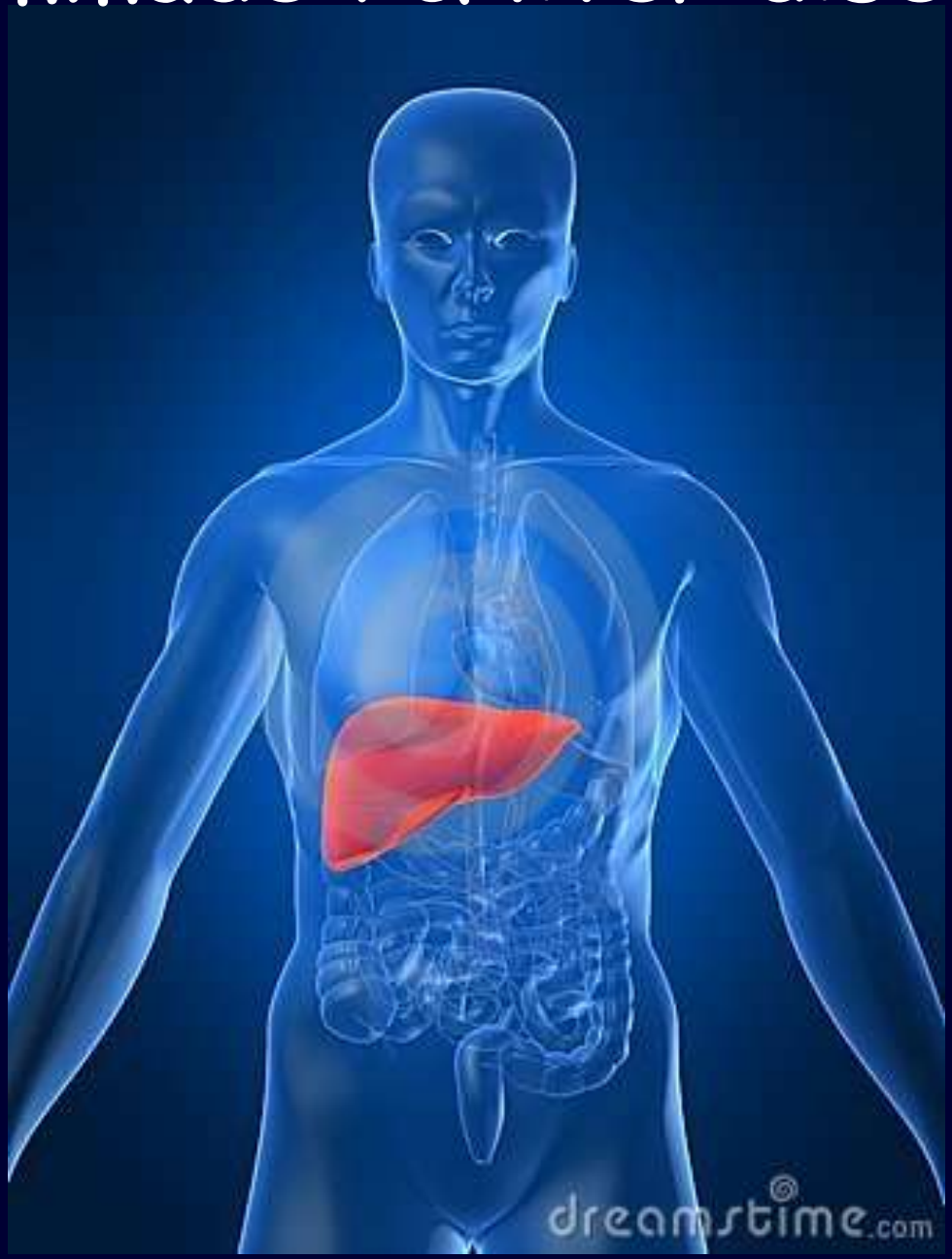
Department of Anaesthetics, Royal Prince Alfred Hospital, Sydney, New South WalesHome

Anaesth Intensive Care. 2011 Mar;39(2):299-302.

Summary

While the pharmacology of sugammadex has been extensively reviewed, there is limited literature regarding its use in specific clinical settings. Authors describe the use of sugammadex in a patient with severe bronchiectasis related to cystic fibrosis who required neuromuscular block for percutaneous endoscopic gastrostomy insertion. The use of rocuronium for neuromuscular block was preferred in order to avoid the potential complications associated with the use of suxamethonium. However, they wished to ensure complete neuromuscular block reversal for this short duration procedure in this high-risk patient and also to avoid the side-effects of traditional reversal agents. Overall, the combination of rocuronium and sugammadex improved perioperative surgical and anaesthetic management in this patient.

Sugammadex & liver diseases



Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2009, **64** (Suppl. 1), pages 55–65

Neuromuscular blocking drugs and their antagonists in patients with organ disease

R. G. Craig[1] and J. M. Hunter[2]

Hepatic disease

To date, no animal studies or clinical trials have been conducted in subjects with hepatic impairment. However, a population pharmacokinetic–pharmacodynamic interaction model of sugammadex has been used to simulate the reversal of rocuronium-induced neuromuscular block in patients with hepatic impairment (data on file with Schering-Plough). Scenarios representing immediate reversal, reversal of profound neuromuscular block, and reversal at reappearance of T2 were simulated in subjects with hepatic impairment. Worst case scenarios, which assume that sugammadex is affected by hepatic impairment, demonstrated that recovery following sugammadex 4 $mg.kg^{-1}$ administered 15 min after rocuronium 1.2 $mg.kg^{-1}$ may take up to 4.12 min longer in patients with severe hepatic impairment than normal patients. When sugammadex 2 $mg.kg^{-1}$ is given at the reappearance of T2, the model predicts that the recovery time will be prolonged by 2.55 min in severe hepatic impairment. Hepatic impairment had little effect on the predicted recovery time after sugammadex 16 $mg.kg^{-1}$ given 3 min after rocuronium. Thus, in patients with hepatic impairment, it could be speculated that recovery after sugammadex will still be faster than after neostigmine, although not as quick as in healthy subjects. The explanation for the findings from these simulations is not yet understood.

In patients with severe hepatic diseases sugammadex should be administered carefully.

Acta Anaesthesiologica Taiwanica 52 (2014) 54–58

Contents lists available at ScienceDirect

Acta Anaesthesiologica Taiwanica

journal homepage: www.e-aat.com

Original Article

Rapid reversal of neuromuscular blockade by sugammadex after continuous infusion of rocuronium in patients with liver dysfunction undergoing hepatic surgery

Ai Fujita [1,2*], Natsuki Ishibe [2], Tatsuya Yoshihara [1], Jun Ohashi [3], Hideichi Makino [4], Mizuko Ikeda [2], Hidekazu Setoguchi [5]

[1] *Department of Clinical Pharmacology, Faculty of Medical Sciences, Kyushu University, Fukuoka, Japan*
[2] *Department of Anesthesiology and Critical Care Medicine, Kyushu University Hospital, Fukuoka, Japan*
[3] *Doctoral Program in Life System Medical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Ibaraki, Japan*
[4] *Shiraishi Hospital Diabetes Center, Imabari, Ehime, Japan*
[5] *Department of Anesthesiology, Kyushu Medical Center, Fukuoka, Japan*

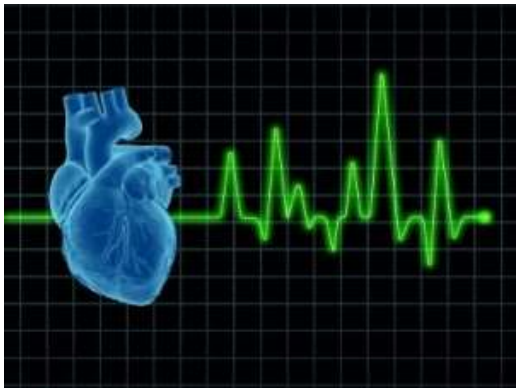
Conclusion: Sugammadex can rapidly reverse NMB after continuous infusion of rocuronium in patients with liver dysfunction undergoing hepatic surgery. Sugammadex was found to be safe and well tolerated. However, further studies of sugammadex under similar conditions should be conducted involving a large number of patients with liver dysfunction undergoing hepatic surgery.

Sugammadex & heart diseases

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2009, **64** (Suppl. 1), pages 55–65

Neuromuscular blocking drugs and their antagonists in patients with organ disease

R. G. Craig[1] and J. M. Hunter[2]

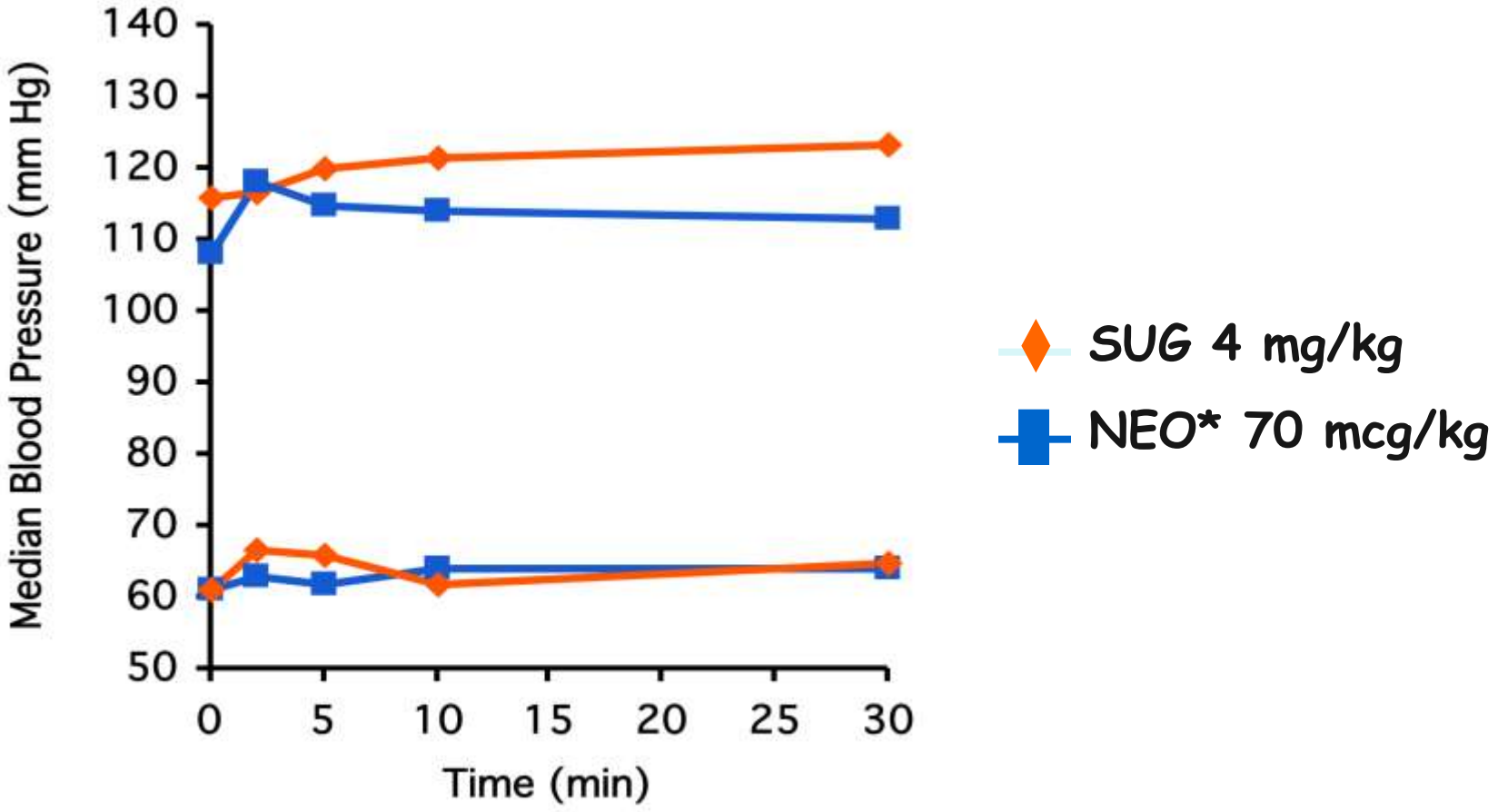


Cardiovascular disease

Dahl et al. [62] studied the efficacy of sugammadex for the reversal of rocuronium-induced neuromuscular block in 76 patients with cardiovascular disease manifesting as ischaemic heart disease, chronic heart failure or arrhythmia (New York Heart Association Class II or III); all patients were undergoing non-cardiac surgery. The control group consisted of patients with a similar degree of cardiovascular disease who were given a placebo (there was no neostigmine group). The study drug was administered at reappearance of T2: 38 patients were given sugammadex 2 mg.kg^{-1}, 38 patients were given sugammadex 4 mg.kg^{-1}, and 40 patients were given placebo. The geometric mean time from the start of administration of the drug to recovery of the TOF ratio to 0.9 was 1.7 min, 1.4 min, and 34.3 min respectively.

There were no statistically significant differences compared to placebo

Reversing Rocuronium 0.6 mg/kg With Sugammadex or Neostigmine From 1 to 2 PTCs: Blood Pressure



*Neostigmine 70 µg/kg combined with glycopyrrolate 14 µg/kg.
NEO, neostigmine; PTC, posttetanic count; SUG. sugammadex

Data from Signal trial.

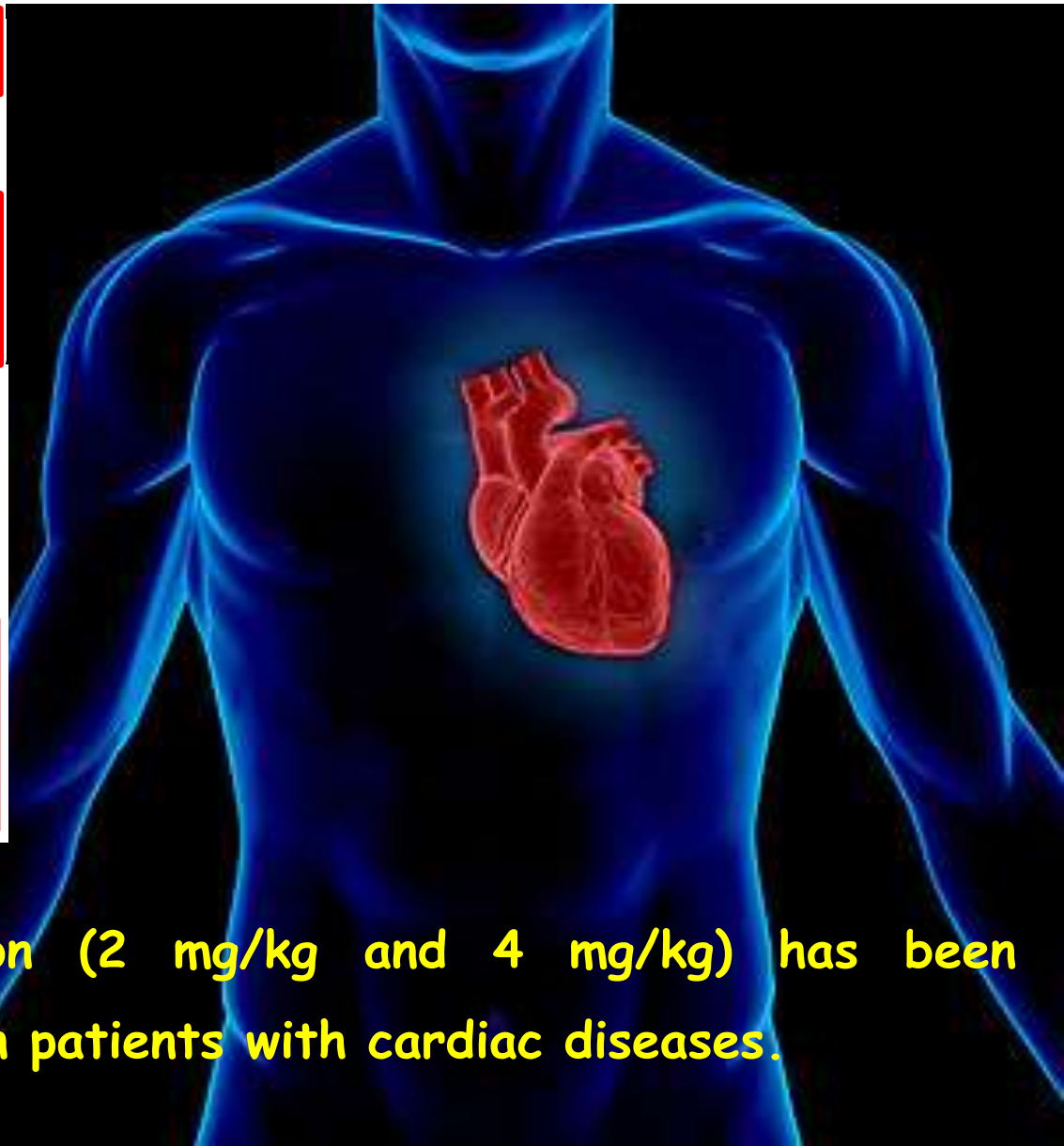
Safety and efficacy of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in cardiac patients undergoing noncardiac surgery

Vegard Dahl[a], Philippe E. Pendeville[b], Markus W. Hollmann[c], Tom Heier[d], Esther A.M. Abels[e] and Manfred Blobner[f]

Background and objective The present randomized, safety-assessor blinded, placebo-controlled trial was designed to assess safety and efficacy of sugammadex, a novel selective relaxant-binding agent, in patients with underlying cardiovascular disease undergoing noncardiac surgery.

Results There were no significant differences between groups in terms of QTc (Fridericia) interval. Three serious adverse events, one in each treatment group, considered to be possibly drug-related according to the investigator, were cases of mild QTc (Bazett) interval prolongation. Blood pressure and heart rate decreased after initiation of anaesthesia and remained stable in all groups up to 10 min after administration of study drug. Blood pressure was significantly higher ($P<0.05$) in both sugammadex dose groups compared with placebo at 30 min. The decrease in heart rate from baseline (prestudy drug) was significantly greater in the 2.0 mg kg^{-1} sugammadex group at 2 and 5 min, and, for both sugammadex groups, the increase at 30 min was greater compared with placebo. Both sugammadex doses resulted in considerably shorter time to recovery of the T4/T1 ratio to 0.9 compared with placebo.

Conclusion The findings indicate sugammadex 2.0 and 4.0 mg kg^{-1} can be given safely and effectively for the reversal of rocuronium-induced neuromuscular blockade in patients with cardiovascular disease undergoing noncardiac surgery. *Eur J Anaesthesiol* 26:874–884 © 2009 European Society of Anaesthesiology.



Sugammadex administration (2 mg/kg and 4 mg/kg) has been demonstrated to be safe in patients with cardiac diseases.

CONCLUSION

Because of alterations in the physiology of the transplanted heart, major consequences related to denervation, variable reinnervation over time, and unexpected side effects of medications like anticholinesterases and anticholinergics can occur perioperatively. Understanding the newly established functions of a transplanted heart, practicing careful anesthetic management and using new reversal agents like sugammadex can provide an uncomplicated perioperative period. Further studies and case reports will help nontransplant specialists, especially, when heart transplant patients present new health problems, sometimes many years after their transplant.

Th ificant side-effects differe

ARTICLE IN PRESS

CASE REPORT

Use of Sugammadex in a Heart Transplant Recipient: A Case Report and Brief Review of the Unique Physiology of the Transplanted Heart

Büşra Tezcan, MD, Alev Şaylan, MD, Demet Bölükbaşı, MD, Rabia Koçulu, MD, and Ümit Karadeniz, MD

Sugammadex & kidneys diseases

British Journal of Anaesthesia **101** (4): 492–7 (2008)
doi:10.1093/bja/aen216 Advance Access publication July 23, 2008

BJA

Multicentre, parallel-group, comparative trial evaluating the efficacy and safety of sugammadex in patients with end-stage renal failure or normal renal function

L. M. Staals[1]*, M. M. J. Snoeck[2], J. J. Driessen[1], E. A. Flockton[3], M. Heeringa[4] and J. M. Hunter[3]

	Impaired renal function *CRCL < 30 ml/min*	*Normal renal function* *CRCL ≥ 80 ml/min*
N	15	14
Median	2.0	1.65
Range	1.2-3.7	0.9-3.1

No significant difference

	Patient group		
	CL_{CR}<30 ml min^{-1} (n=15)	CL_{CR}≥80 ml min^{-1} (n=14)*	ANOVA
Recovery to TOF ratio 0.7, mean (SD)	1.45 (0.47)	1.17 (0.38)	NS
Recovery to TOF ratio 0.8, mean (SD)	1.60 (0.57)	1.32 (0.45)	NS
Recovery to TOF ratio 0.9, mean (SD)	2.00 (0.72)	1.65 (0.63)	NS

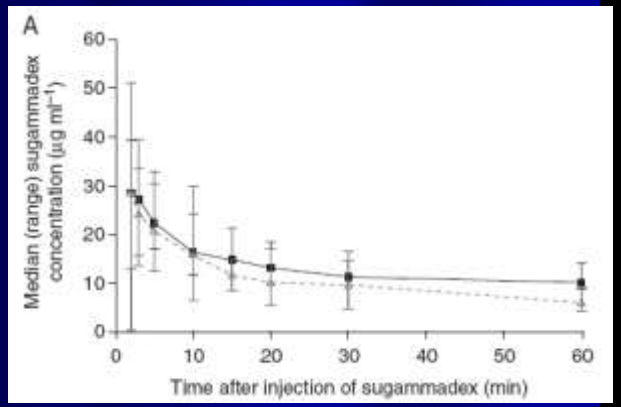
Conclusions. Sugammadex administered at reappearance of T_2 rapidly and effectively reverses NMB induced by rocuronium in renal failure and healthy patients. Sugammadex was well tolerated by all patients. Further safety studies on sugammadex in patients with severe renal impairment are warranted.

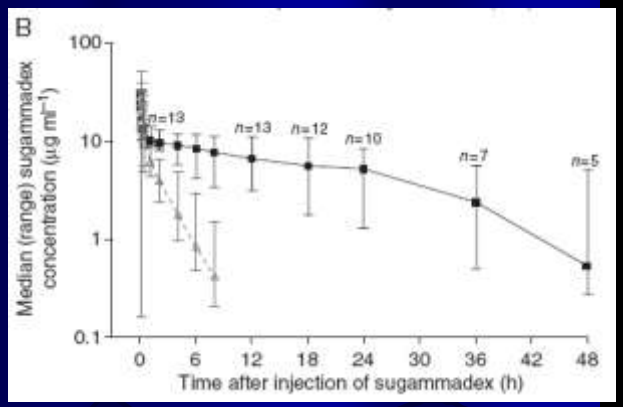
British Journal of Anaesthesia **104** (1): 31–9 (2010)
doi:10.1093/bja/aep340

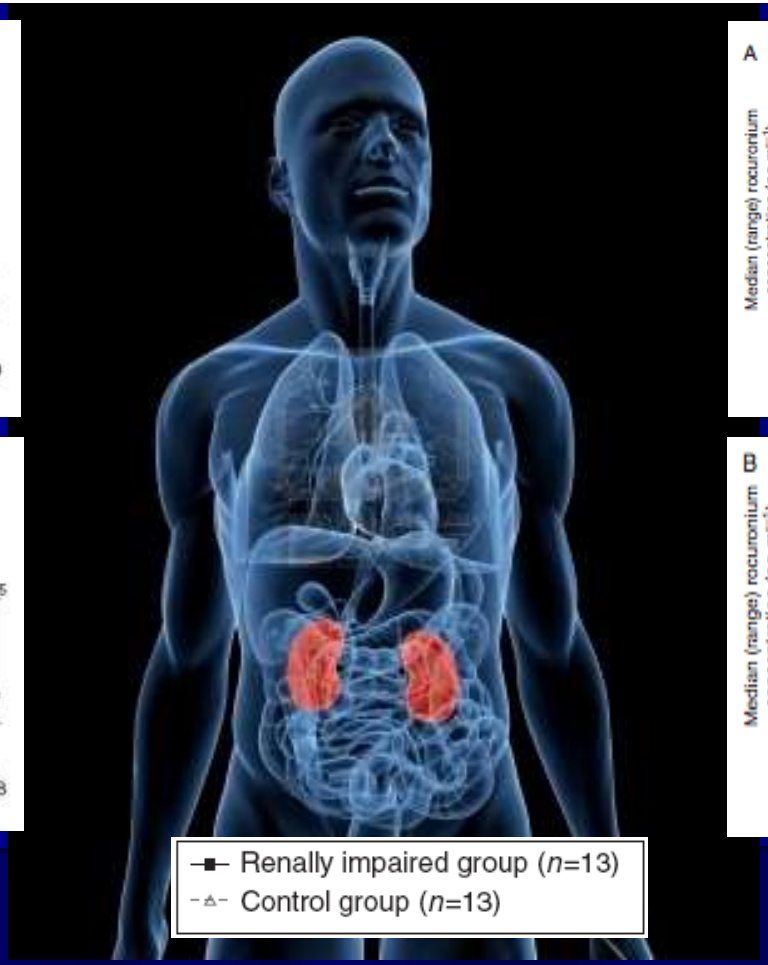
BJA

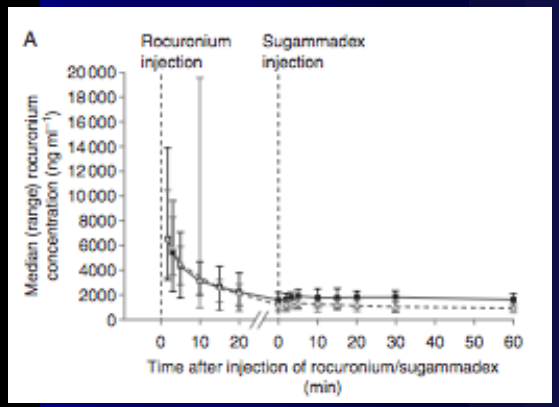
Reduced clearance of rocuronium and sugammadex in patients with severe to end-stage renal failure: a pharmacokinetic study†

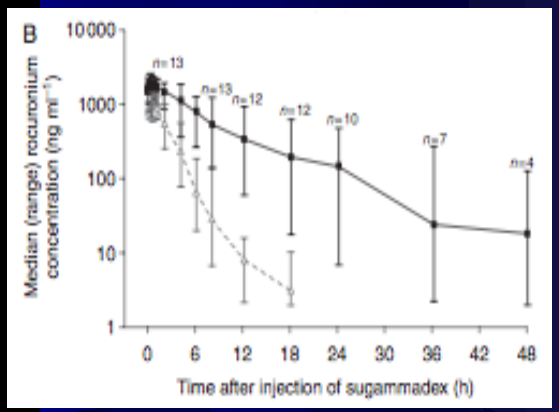
L. M. Staals[1]*, M. M. J. Snoeck[3], J. J. Driessen[1], H. W. van Hamersvelt[2], E. A. Flockton[4], M. W. van den Heuvel[5] and J. M. Hunter[4]











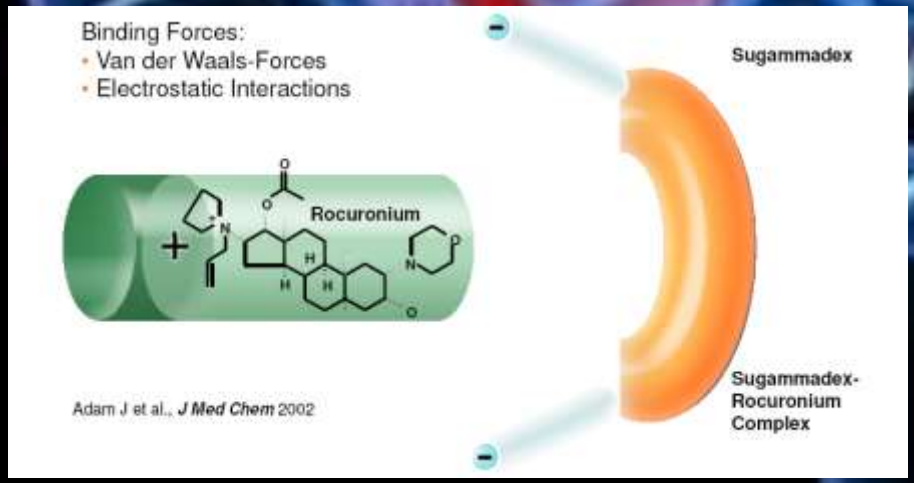
Sugammadex

Rocuronium

KEY POINTS

After administration of sugammadex, the concentration of rocuronium showed a plateau or even an increase.

Available evidence suggests that the rocuronium-sugammadex complex remains stable over time. The sugammadex-rocuronium complex exists in equilibrium with a very low dissociation rate ($K_d = 0{,}1 \times 10^{-6} M$) because of strong binding.



Naguib M. Sugammadex: another milestone in clinical neuromuscular pharmacology. *Anesth Analg* 2007; 104: 575–81

BJA

British Journal of Anaesthesia 114 (5): 777–784 (2015)

doi: 10.1093/bja/aet586
Advance Access Publication 31 March 2015
Article

ARTICLE

Efficacy, safety and pharmacokinetics of sugammadex 4 mg kg^{-1} for reversal of deep neuromuscular blockade in patients with severe renal impairment

I. F. Panhuizen[1], S. J. A. Gold[2], C. Buerkle[3], M. M. J. Snoeck[1,*], N. J. N. Harper[2], M. J. G. H. Kaspers[4], M. W. van den Heuvel[4], and M. W. Hollmann[5]

[1]Department of Anaesthesia, Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands, [2]Department of Anaesthesia, Central Manchester University Hospitals NHS Foundation Trust UK, Manchester, UK, [3]Department of Anaesthesia and Intensive Care Medicine, Feldkirch Hospital, Austria, [4]MSD, Oss, The Netherlands, and [5]Department of Anaesthesiology, University of Amsterdam (AMC), Amsterdam, The Netherlands

British Journal of Anaesthesia **109** (3): 382–90 (2012)
Advance Access publication 24 June 2012 · doi:10.1093/bja/aes207

BJA

Dialysability of sugammadex and its complex with rocuronium in intensive care patients with severe renal impairment

G. Cammu[1*], B. Van Vlem[2], M. van den Heuvel[4], L. Stet[5], R. el Galta[6], S. Eloot[2] and I. Demeyer[3]

[1] Department of Anaesthesiology and Critical Care Medicine, [2] Renal Unit, and [3] Department of Emergency Medicine, Onze-Lieve-Vrouw Ziekenhuis, Moorselbaan 164, 9300 Aalst, Belgium
[4] Clinical PKPD, [5] CNS Global Clinical Trial Management, and [6] Biostatistics and Research Decision Sciences, MSD, Oss, The Netherlands

Conclusions. Haemodialysis using a high-flux dialysis method is effective in removing sugammadex and the sugammadex–rocuronium complex in patients with severe renal impairment.

Sugammadex & bleeding

Ann Fr Anesth Reanim. 2011 Oct;30(10):714-7. doi: 10.1016/j.annfar.2011.04.019. Epub 2011 Jul 7.

[Clinical evaluation of post-surgical bleeding after a sugammadex injection].

[Article in French]

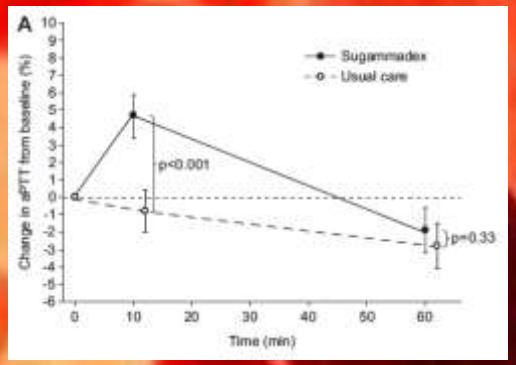
Raft J[1], Betala Belinga JF, Jurkolow G, Desandes E, Longrois D, Meistelman C.

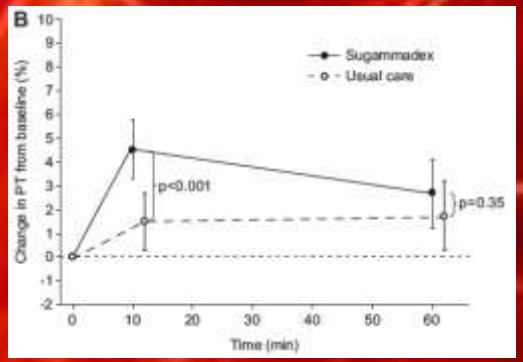
⊕ **Author information**

Conclusion: in this retrospective study on patients at high risk for postoperative bleeding, sugammadex at 2 e 4 mg/Kg doses was not associated with higher risk for bleeding.
Patients who receive higher doses of sugammadex (> 4mg/kg) or patients with altered coagulation profiles should be analysed.

Effect of Reversal of Neuromuscular Blockade with Sugammadex *versus* Usual Care on Bleeding Risk in a Randomized Study of Surgical Patients

Niels Rahe-Meyer, M.D., Ph.D., Hein Fennema, Ph.D., Sam Schulman, M.D., Ph.D., Walter Klimscha, M.D., Michael Przemeck, M.D., Manfred Blobner, M.D., Hinnerk Wulf, M.D., Marcel Speek, R.N., C.R.N.A., Christine McCrary Sisk, B.S., Debora Williams-Herman, M.D., Tiffany Woo, M.S., Armin Szegedi, M.D., Ph.D.





Results: Of 1,198 patients randomized, 1,184 were treated (sugammadex n = 596, usual care n = 588). Bleeding events within 24 h (classified by an independent, blinded Adjudication Committee) were reported in 17 (2.9%) sugammadex and 24 (4.1%) usual care patients (relative risk [95% CI], 0.70 [0.38 to 1.29]). Compared with usual care, increases of 5.5% in activated partial thromboplastin time ($P < 0.001$) and 3.0% in prothrombin time ($P < 0.001$) from baseline with sugammadex occurred 10 min after administration and resolved within 60 min. There were no significant differences between sugammadex and usual care for other blood loss measures (transfusion, 24-h drain volume, drop in hemoglobin, and anemia), or risk of venous thromboembolism, and no cases of anaphylaxis.

Conclusion: Sugammadex produced limited, transient (<1 h) increases in activated partial thromboplastin time and prothrombin time but was not associated with increased risk of bleeding *versus* usual care. **(ANESTHESIOLOGY 2014; 121:969-77)**

Sugammadex and anaphylaxis

Abstract

Anaesthesia. 2014 Nov;69(11):1251-7. doi: 10.1111/anae.12736. Epub 2014 May 22.

Hypersensitivity associated with sugammadex administration: a systematic review.

Tsur A[1], Kalansky A.

Summary

Sugammadex is a drug used to reverse neuromuscular blockade induced by rocuronium or vecuronium. It has not yet been approved by the Food and Drug Administration in the USA due to concerns regarding hypersensitivity. The objective of this review was to identify similarities in the presentation of hypersensitivity reactions to sugammadex. A comprehensive search was performed in PubMed, Scopus and Web of Science for cases reporting hypersensitivity reactions to sugammadex. In addition, we contacted regulatory agencies and the company marketing the drug for unpublished reports. Reports were included if they were in English, primary investigations, lacked an alternative probable explanation for the reaction and included a comprehensive description of the hypersensitivity. We identified 15 cases of hypersensitivity following sugammadex administration. All cases that reported exact timing (14/15) occurred in 4 min or less. Most of the patients (11/15; 73%) met World Anaphylaxis Organization criteria for anaphylaxis. Awareness must be raised for the possibility of drug-induced hypersensitivity during the critical 5-min period immediately following sugammadex administration.

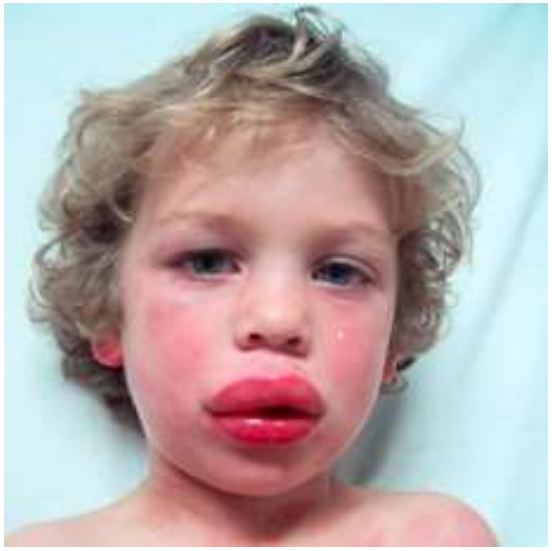
Abstract

Background: Sugammadex has a unique mechanism of action and is widely used because of its safety and efficacy. A few recent reports have described allergic reactions to clinical doses of sugammadex. We hereby describe another series of cases of possible anaphylaxis to sugammadex.

Case presentation: We present three suspected cases of sugammadex-induced anaphylactic shock, including a 13-year-old boy who underwent laparoscopic appendectomy, a 75-year-old woman who underwent left knee arthroplasty, and a 34-year-old man who underwent left pansinectomy for sinobronchitis. All three patients received general anesthesia with rocuronium and their tracheas were intubated. Shortly after injection of sugammadex for reversal of rocuronium, all of them experienced a decrease in blood pressure along with mucocutaneous erythema. In the most severe case, reintubation after extubation was required due to difficulty in manual ventilation. All patients recovered with anti-allergic therapy. On later investigation, all three patients had a positive skin reaction to sugammadex.

Conclusion: Our results suggest that physicians using sugammadex should be aware of the possibility of sugammadex-induced anaphylaxis.

Keywords: Sugammadex, Anaphylactic shock, General anesthesia



Case Report **Open Access**

Acute Cardiac Failure after Muscle Block Reversal with Sugammadex for Unexpected Difficult Intubation

Carmelina Gurrieri, Paolo Murabito, Giovanni Buscema, Danilo Grasso, Marinella Astuto
Department of Anesthesiology and Intensive Care, Policlinico-Vittorio Emanuele University Hospital, via Santa Sofia 78, 95123 Catania, Italy

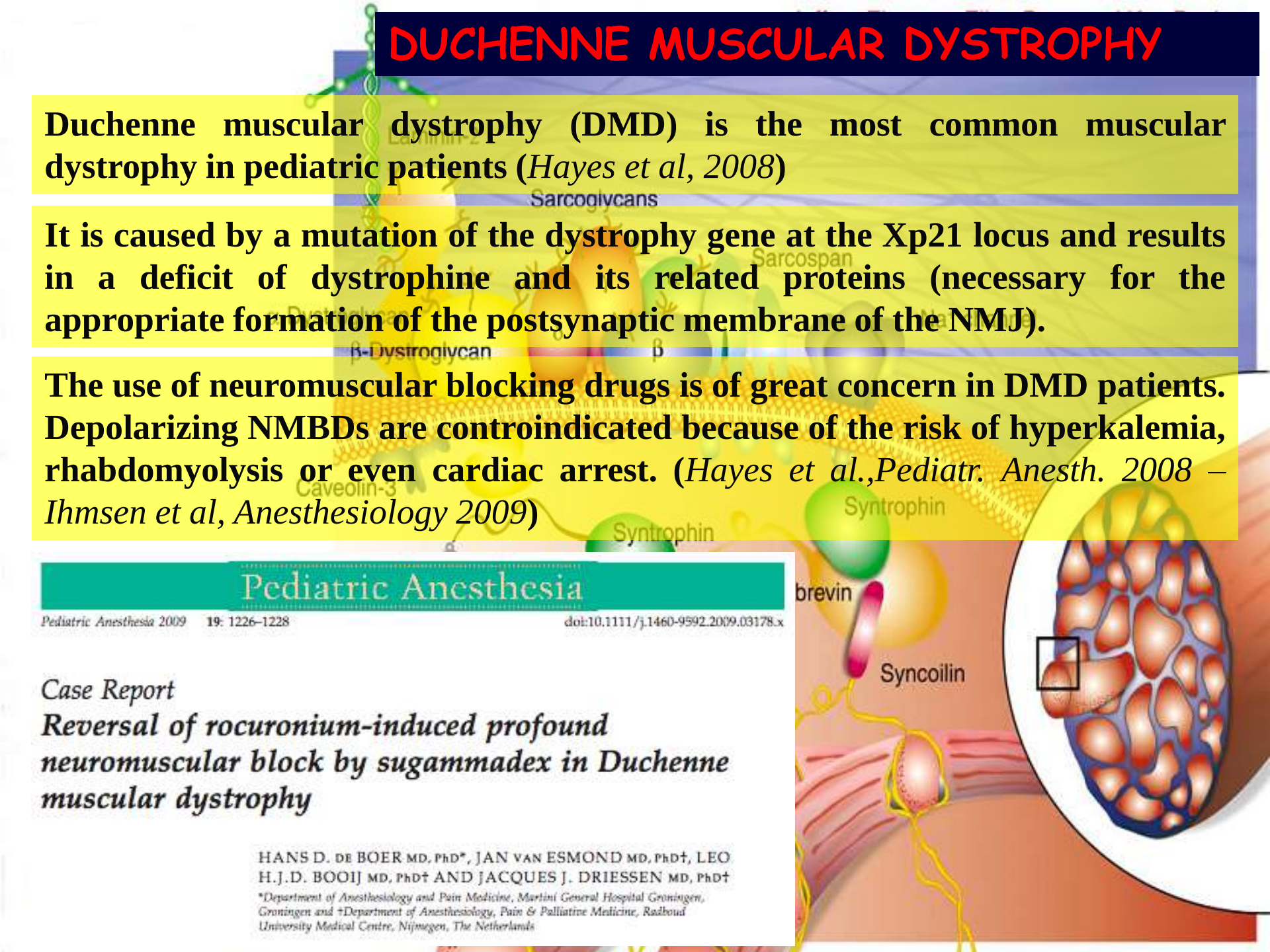
Sugammadex in special clinical settings

DUCHENNE MUSCULAR DYSTROPHY

Duchenne muscular dystrophy (DMD) is the most common muscular dystrophy in pediatric patients (*Hayes et al, 2008*)

It is caused by a mutation of the dystrophy gene at the Xp21 locus and results in a deficit of dystrophine and its related proteins (necessary for the appropriate formation of the postsynaptic membrane of the NMJ).

The use of neuromuscular blocking drugs is of great concern in DMD patients. Depolarizing NMBDs are controindicated because of the risk of hyperkalemia, rhabdomyolysis or even cardiac arrest. (*Hayes et al.,Pediatr. Anesth. 2008 – Ihmsen et al, Anesthesiology 2009*)



Pediatric Anesthesia

Pediatric Anesthesia 2009 **19**: 1226–1228 doi:10.1111/j.1460-9592.2009.03178.x

Case Report

Reversal of rocuronium-induced profound neuromuscular block by sugammadex in Duchenne muscular dystrophy

HANS D. DE BOER MD, PhD*, JAN VAN ESMOND MD, PhD†, LEO H.J.D. BOOIJ MD, PhD† AND JACQUES J. DRIESSEN MD, PhD†

**Department of Anesthesiology and Pain Medicine, Martini General Hospital Groningen, Groningen and †Department of Anesthesiology, Pain & Palliative Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands*

MYASTHENIA GRAVIS

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2010, 65, pages 302–305 doi:10.1111/j.1365-2044.2009.06236.x

CASE REPORTS

The use of sugammadex in a patient with myasthenia gravis

C. Unterbuchner,[1] H. Fink[2] and M. Blobner[3]

1 Resident, 2 Associate Professor of Anaesthesia, 3 Professor of Anaesthesia, Klinik für Anaesthesiologie, Klinikum rechts der Isar, Technische Universität München, München, Germany

LETTER TO THE EDITOR

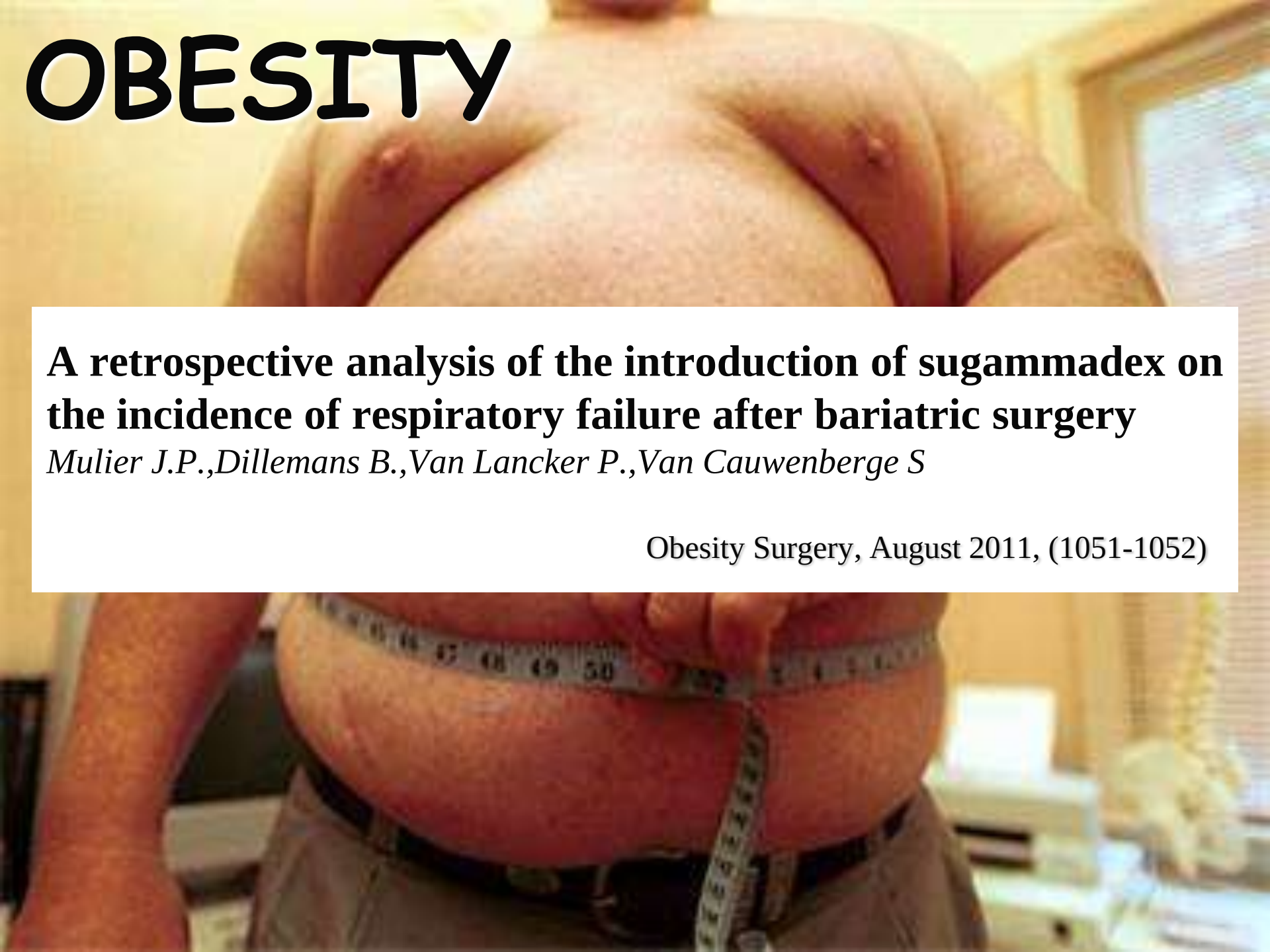
Reversal of neuromuscular blockade with sugammadex in an obese myasthenic patient undergoing thymectomy

Helena Argiriadou · Kyriakos Anastasiadis · Evanthia Thomaidou · Dimitrios Vasilakos

MG is an autoimmune disease affecting neuromuscular trasmission.

Auto antibodies against the acetylcholine receptor reduce the total amount of Ach receptors resulting in an unpredictable response to administered neuromuscolar blocking drugs. (*Paton WD, The Journal of Physiology 1967*)

OBESITY



A retrospective analysis of the introduction of sugammadex on the incidence of respiratory failure after bariatric surgery

Mulier J.P.,Dillemans B.,Van Lancker P.,Van Cauwenberge S

Obesity Surgery, August 2011, (1051-1052)

DOSAGE ???

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

Anaesthesia, 2011, **66**, pages 721–725 doi:10.1111/j.1365-2044.2011.06782.x

ORIGINAL ARTICLE

Ideal versus corrected body weight for dosage of sugammadex in morbidly obese patients

P. Van Lancker,[1] B. Dillemans,[2] T. Bogaert,[3] J. P. Mulier,[1] M. De Kock[4] and M. Haspeslagh[5]

1 Specialist Anaesthetist, 3 Resident Anaesthetist, Department of Anaesthesia, 2 Specialist Surgeon, Department of Surgery, 5 Biostatistics and Clinical Research Associate, AZ Sint-Jan Brugge-Oostende AV, Belgium
4 Professor of Anaesthesia, Dep

Summary

To date, the dosing of sugammadex is based on real body weight without taking fat content into account. We compared the reversal of profound rocuronium-induced neuromuscular blockade in morbidly obese patients using doses of sugammadex based on four different weight corrections. One hundred morbidly obese patients, scheduled for laparoscopic bariatric surgery under propofol-sufentanil anaesthesia, were randomly assigned four groups: ideal body weight; ideal body weight + 20%; ideal body weight + 40%; and real body weight. Patients received sugammadex 2 $mg.kg^{-1}$, when adductor pollicis monitoring showed two responses. The primary endpoint was full decurarisation. Secondary endpoints were the ability to get into bed independently on arrival to the post-anaesthetic care unit and clinical signs of residual paralysis. There was no residual paralysis in any patient. Morbidly obese patients can safely be decurarised from rocuronium-induced neuromuscular blockade T1–T2 with sugammadex dosed at 2 $mg.kg^{-1}$ ideal body weight + 40% ($p < 0.0001$).

Conclusion: A sugammadex dose calculated according to IBW

We conclude that sugammadex cannot be safely calculated for morbidly obese patients on the basis of IBW. Until a dose regimen that works well in the majority of morbidly obese patients is established, we can expect to see a large number of slow responders and even outliers. The implication seems to be that neuromuscular monitoring of depth is necessary in the morbidly obese so that a second dose of sugammadex can be given as soon as it is clear that response is slow.

Sugammadex Ideal Body Weight Dose Adjusted by Level of Neuromuscular Blockade in Laparoscopic Bariatric Surgery

Sandra Llauradó, M.D.,* Antoni Sabaté, M.D., Ph.D.,† Eva Ferreres, M.D.,* Inmaculada Camprubí, M.D.,* Anna Cabrera, M.D.*

Anesthesiology, V 117 • No 1 July 2012

PREGNANCY

Acta Anaesthesiol Scand 2011; ■■: 1–6
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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2011.02431.x

Rocuronium and sugammadex for rapid sequence induction of obstetric general anaesthesia

R. M. WILLIAMSON, S. MALLAIAH and P. BARCLAY
Liverpool Women's Hospital, Liverpool, UK

encapsulation of rocuronium in the plasma in various groups of patients. We reported seven Caesarean section cases, undergoing general anaesthesia with thiopental (6 mg kg^{-1}) and rocuronium (0.6 mg kg^{-1}) who were given desflurane and fentanyl for maintenance of anaesthesia after delivery. The action of rocuronium may be prolonged in pregnant women. At the end of the operation, all patients had a significant degree of neuromuscular block. In five patients, there was no single twitch response and no TOF ratio, one patient had one twitch detectable, and in one

kg^{-1}) was given. In all patients, sugammadex provided rapid and sufficient reversal to TOF >0.9 within 2 min. All patients were monitored after operation, and no signs of recurarization occurred in any patient and no signs of neuromuscular weakness were observed.

British Journal of Anaesthesia **108** (4): 612–14 (2012)
Advance Access publication 26 January 2012 · doi:10.1093/bja/aer494

Case report

Use of sugammadex in a 'can't intubate, can't ventilate' situation

R. Curtis, S. Lomax and B. Patel*

Department of Anaesthesia, Royal Surrey County Hospital, Guildford GU2 7XX, UK

* Corresponding author. E-mail: bhavesh.patel@nhs.net

Editor's key points

- Sugammadex reversal of rocuronium has been suggested for management of a difficult airway.
- In a patient with upper airway pathology, attempts at tracheal intubation resulted in a 'can't intubate, can't ventilate' situation.
- Sugammadex reversed the rocuronium but did not restore airway patency.
- Alternative strategies for airway management must be immediately available.

Anaesth Intensive Care. 2012 Jul;40(4):722.

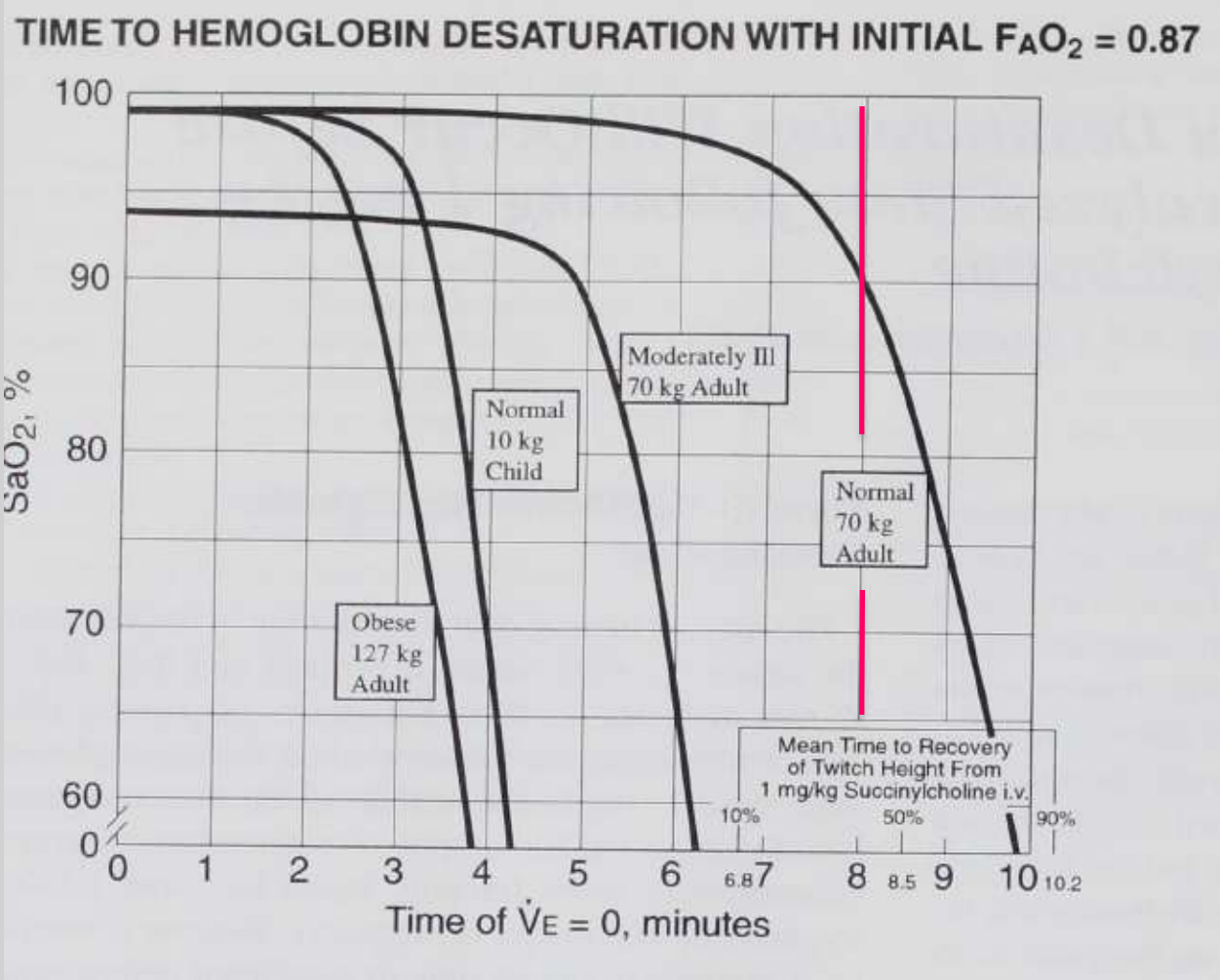
Persistent 'can't intubate, can't oxygenate' crisis despite reversal of rocuronium with sugammadex: the importance of timing.

Curtis RP.

Anesthesiology
1997; 87:979–82

Critical Hemoglobin Desaturation Will Occur before Return to an Unparalyzed State following 1 mg/kg Intravenous Succinylcholine

Jonathan L. Benumof, M.D., Rachel Dagg, M.S.,† Reuben Benumof, Ph.D.‡*



"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."