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# The best practice in the neuromuscular blockade management

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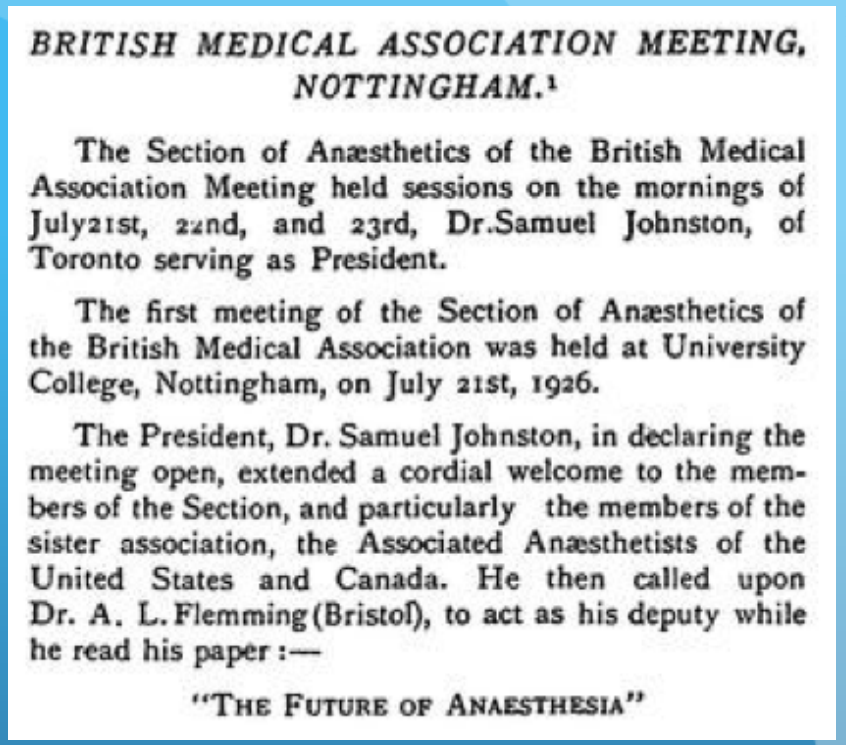
Saint Petersburg 2012



# The Benefits of Neuromuscular Blockade 1926





*BRITISH MEDICAL ASSOCIATION MEETING, NOTTINGHAM.*[1]

The Section of Anæsthetics of the British Medical Association Meeting held sessions on the mornings of July21st, 22nd, and 23rd, Dr.Samuel Johnston, of Toronto serving as President.

The first meeting of the Section of Anæsthetics of the British Medical Association was held at University College, Nottingham, on July 21st, 1926.

The President, Dr. Samuel Johnston, in declaring the meeting open, extended a cordial welcome to the members of the Section, and particularly the members of the sister association, the Associated Anæsthetists of the United States and Canada. He then called upon Dr. A. L. Flemming (Bristol), to act as his deputy while he read his paper :—

"THE FUTURE OF ANAESTHESIA"

- 1926: Annual meeting BMA,Nottingham:
  - Samuel Johnston, President of the section of Anaesthetics:
    - "For once there could be an association of surgery and anaesthesia without the question of sufficient relaxation arising"

# The Benefits of Neuromuscular Blockade since 1942

THE USE OF CURARE IN GENERAL ANESTHESIA

HAROLD R. GRIFFITH, M.D., AND G. ENID JOHNSON, M.D.*

*Montreal, Canada*

***Anesthesiology* 1942;3:418-20**

The use of curare in 25 patients by Harold Griffith and Enid Johnson in 1942 changed anesthetic practice throughout the world and heralded the start of the modern era of anesthesiology. The introduction of curare allowed adequate muscle relaxation at a lighter, and therefore better-tolerated, degree of general anesthesia.

Many allergic reactions, no short onset, long acting NMB, no good reversal

No good muscle relaxation possible

# New non depolarizing NMB were introduced.

**Table 1. Main neuromuscular features of the new relaxants in comparison to pancuronium, atracurium and vecuronium.**

| | $ED_{50}$ (μg/kg) | Intubating dose (mg/kg) | Onset time of the intubating dose (min) | Duration of clinical relaxation (min) |
|---|---|---|---|---|
| ~~Doxacurium~~ | 30 | 0.03–0.05 | 5–10 | 50–150 |
| ~~Pipecuronium~~ | 45 | 0.05–0.07 | 4– 7 | 45–100 |
| ~~Mivacurium~~ | 70 | 0.15–0.2 | 2– 4 | 15– 20 |
| Rocuronium | 300 | 0.5– 0.6 | 1– 2 | 25– 35 |
| ~~Pancuronium~~ | 60 | 0.08–0.1 | 3– 5 | 50–100 |
| ~~Atracurium~~ | 225 | 0.4– 0.5 | 2– 4 | 25– 35 |
| ~~Vecuronium~~ | 40 | 0.08–0.1 | 2– 4 | 25– 35 |

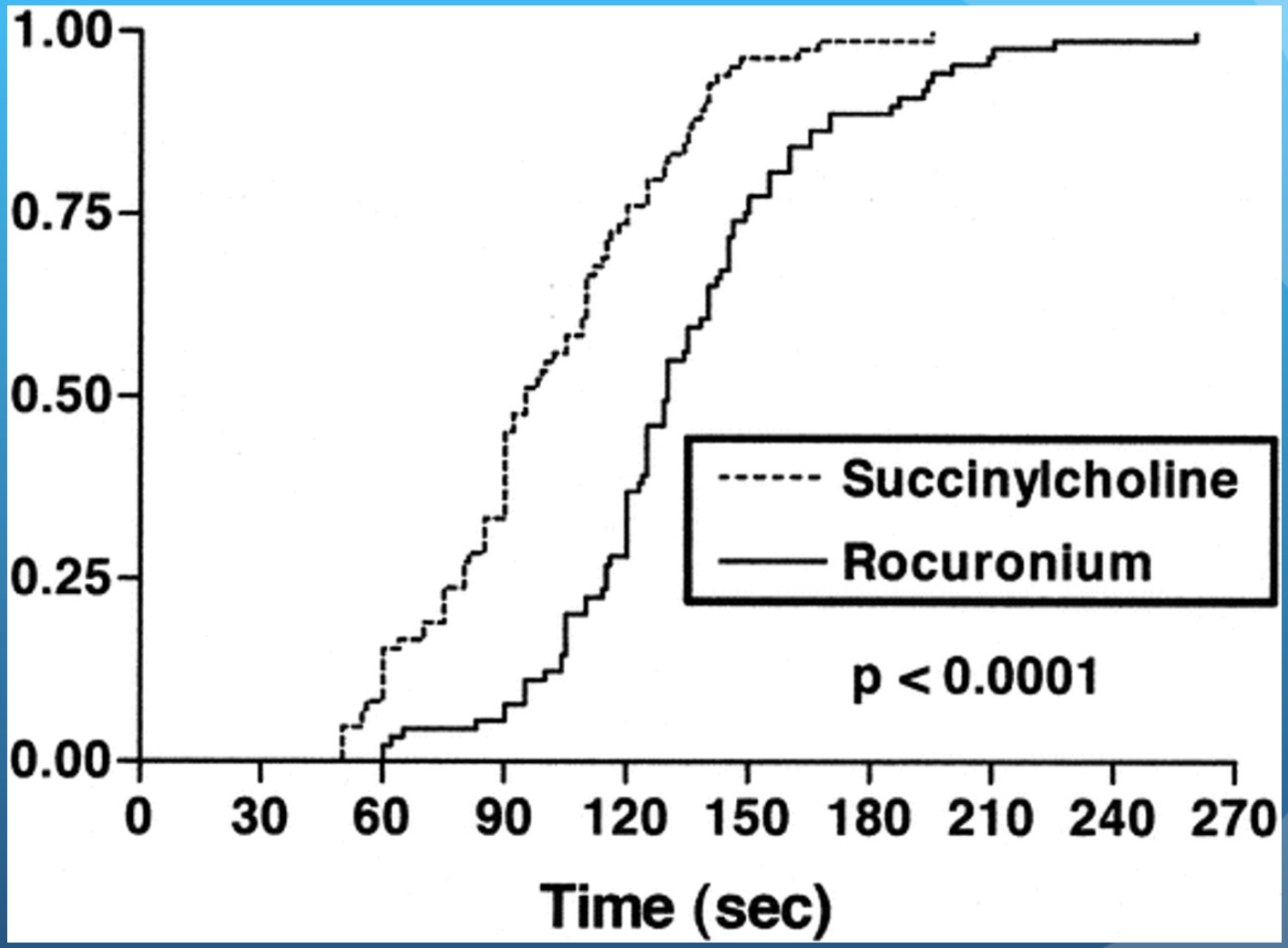
The variability in the onset times and the duration of clinical relaxation is greater in agents which are slower in onset and longer acting.

The weakest NMBA's have the best predictable short onset time and shortest duration

# Lowest renal excretion improves Predictable duration.

| Modes of Elimination | | | |
|---|---|---|---|
| Drug | Percentage Elimination | | |
| | Renal | Hepatic | Metabolic |
| Alcuronium | 70-90 | 10-30 | 0 |
| Atracurium | < 10 | 0 | > 90 |
| Gallamine | 100 | 0 | 0 |
| Pancuronium | 30-80 | 10 | 15-40 |
| Tubocurarine | 40-60 | 40-60 | 0 |
| Vecuronium | > 25 | 20 | 50-60 |
| Pipecuronium | 60-90 | 10-40 | - |
| Doxacurium | 60-90 | 10-40 | - |
| Rocuronium | 10-20 | 80-90 | - |
| Mivacurium | | | +++ |

# Probability of endotracheal intubation after succinylcholine or rocuronium.

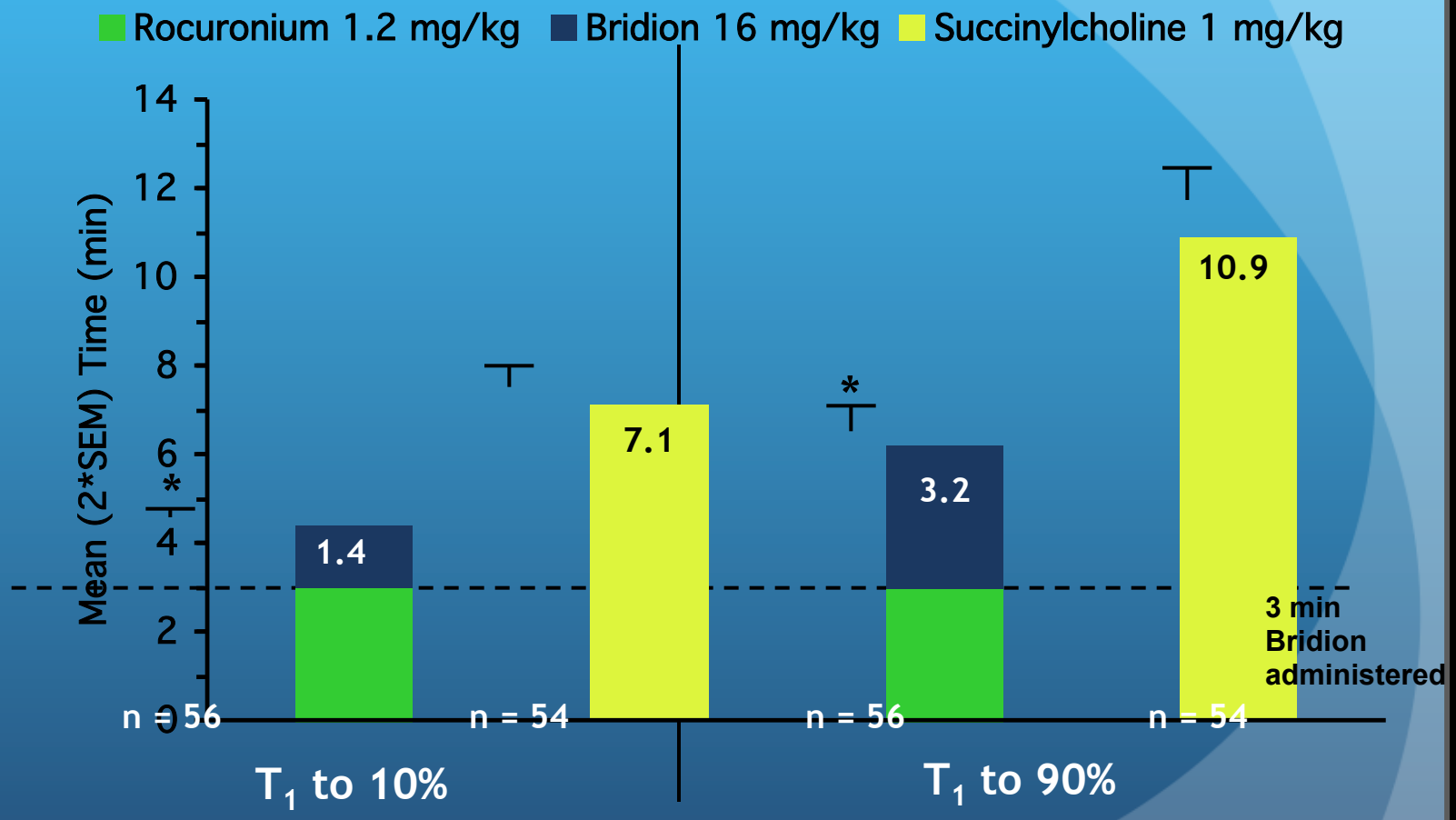



Sluga M et al. Anesth Analg 2005;101:1356-1361

# Rocuronium = or ? > Succinylcholine

- Mencke T Anesth Analg. 2006;102:943 **Rocuronium is not associated with more vocal cord injuries than succinylcholine after rapid-sequence induction: a randomized, prospective, controlled trial.**
  - The incidence and severity of sore throat and myalgia were were comparable.
- Tang L Acta Anaesthesiol Scand. 2011;55:203 **Desaturation following rapid sequence induction using succinylcholine vs. rocuronium in overweight patients.**
  - Succinylcholine was associated with a significantly more rapid desaturation and longer recovery of oxygen saturation than rocuronium during rapid sequence induction in overweight patients.

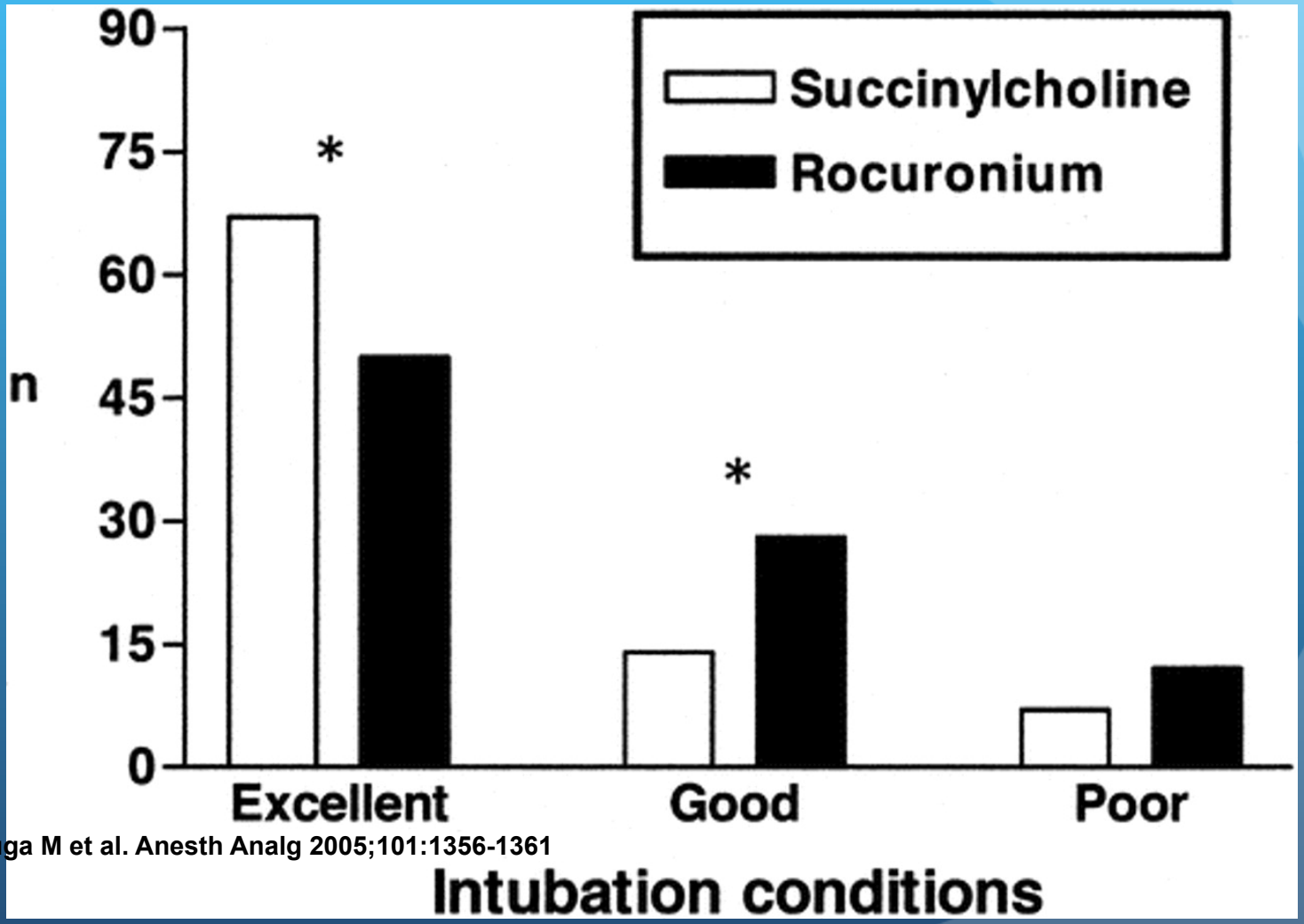
# Immediate Reversal of Intense Blockade




*$P$ < 0.0001 versus succinylcholine treatment group; results based on intent-to-treat population.
SEM, standard error of mean.

Data from Spectrum trial.

# Endotracheal intubation conditions during rapid sequence induction of anesthesia with succinylcholine or rocuronium.

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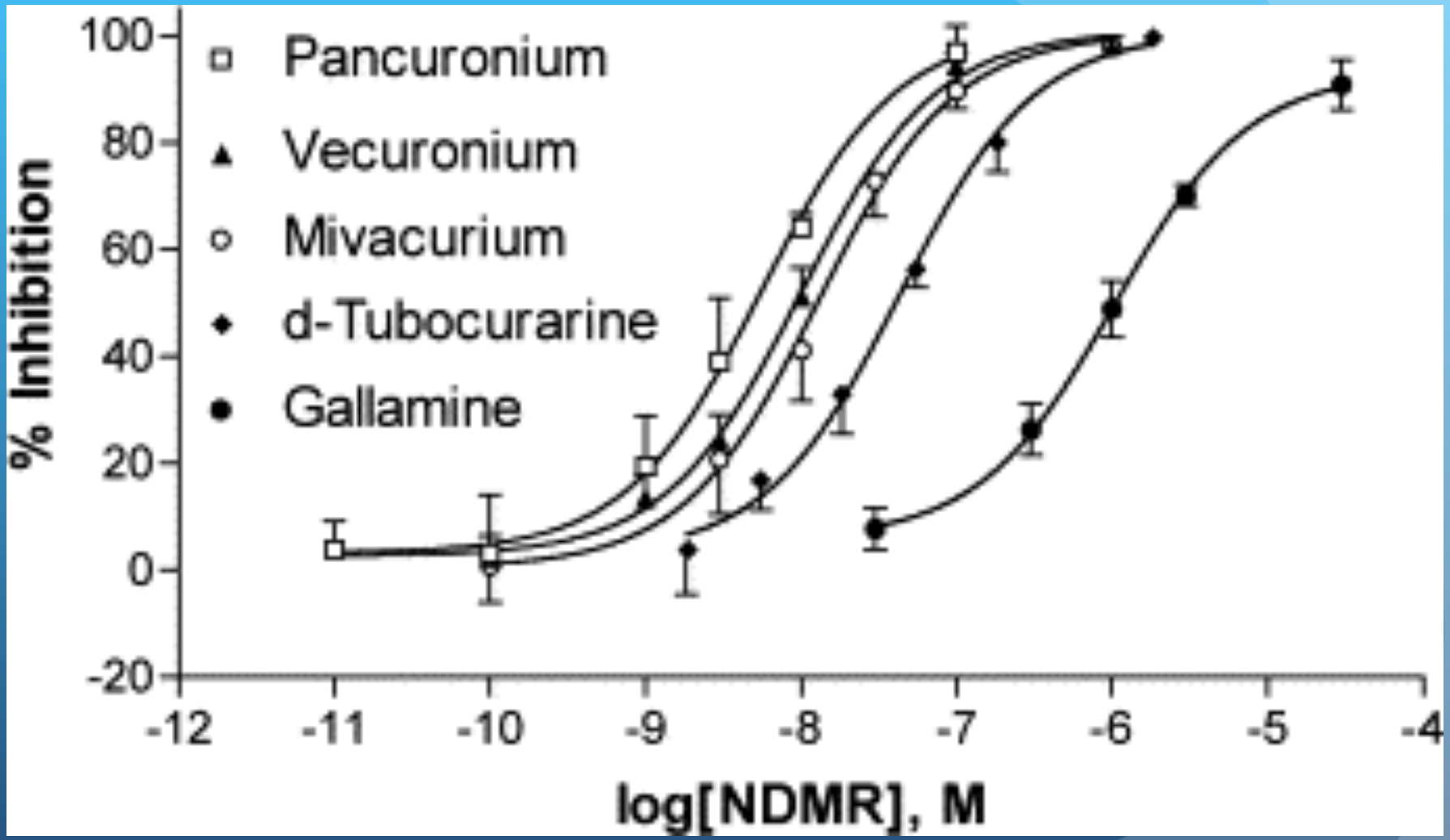

Pancuronium
Vecuronium
Mivacurium
d-Tubocurarine
Gallamine
% Inhibition
100
80
60
40
20
0
-20
-12
-11
-10
-9
-8
-7
-6
-5
-4
log[NDMR], M

# How do you measure NMB reversal?

1. Wait long enough after last dose NMB.
2. Patient is able to breath spontaneously with large tidal volumes.
3. Patient is able to squeeze your hand for more than 5 s.
4. Patient is able to lift his head for more than 5 s.
5. Patient is able to breath spontaneously without obstruction when extubated.

   This is all wrong and might lead to insufficient reversal

# PORC (Post operative residual curarisation) remains high whatever NMBA you use



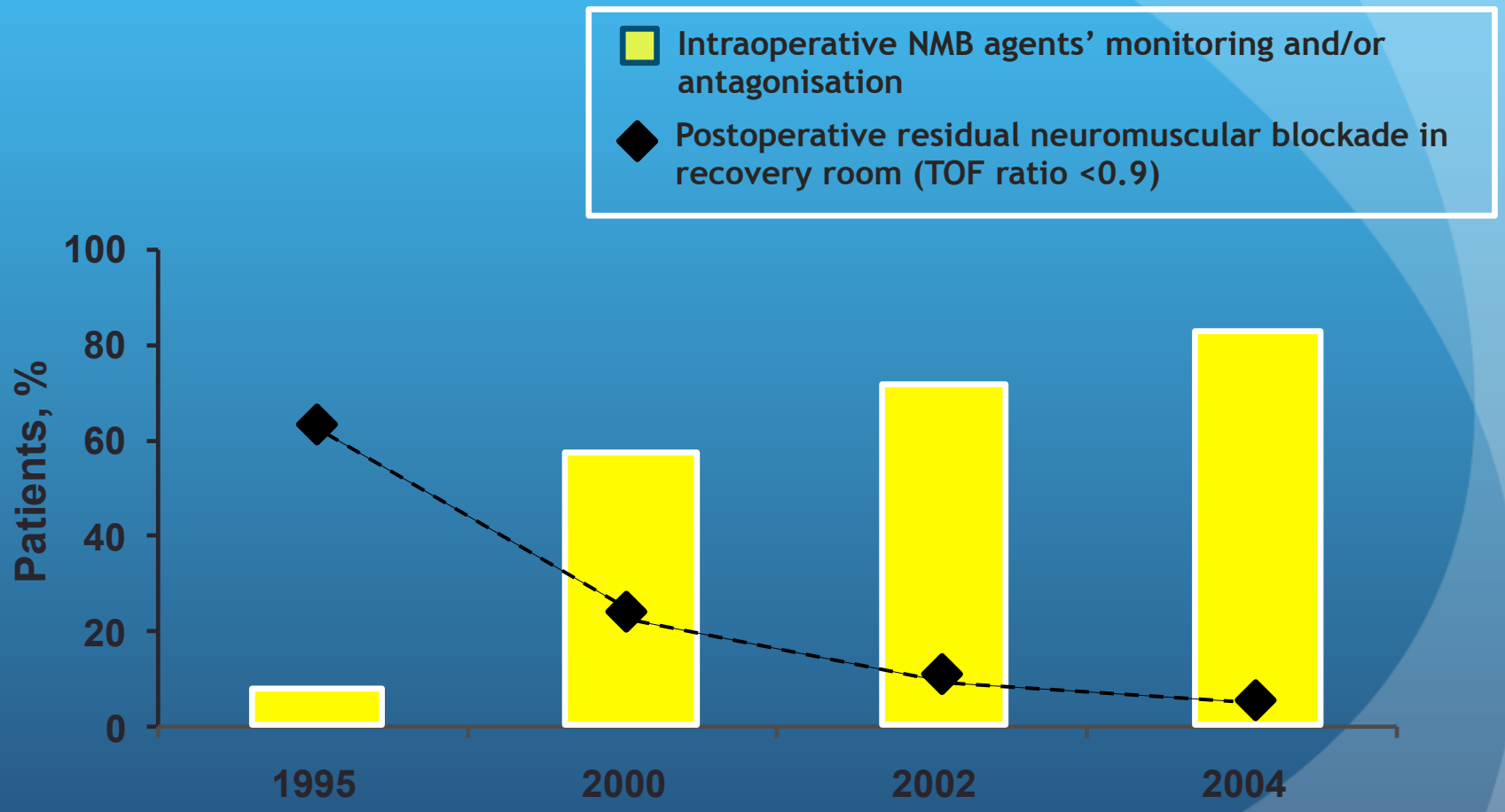
**Table 1.** Patients (%) With Train-of-Four (TOF) <90% - Frequency Distribution of Neuromuscular Blocking Drug (NMBD) Given at Induction of Anesthesia, Frequency Distribution of the Intraoperative Variables Examined Before Tracheal Extubation, and Distribution of a Tympanic Temperature <36°C at Arrival in the Postanesthetic Care Unit (PACU)

| | Outpatients | Outpatients with TOF <90% | Inpatients | Inpatients with TOF <90% |
|---|---|---|---|---|
| NMBD | | | | |
| Atracurium | 23% (75/320) | 51% (38/75) | 36% (114/320) | 43% (49/114) |
| Cisatracurium | 2% (6/320) | 33% (2/6) | 2% (8/320) | 62% (5/8) |
| Mivacurium | 50% (160/320) | 23% (37/160) | 15% (48/320) | 35% (17/48) |
| Rocuronium | 22% (71/320) | 39% (28/71) | 44% (141/320) | 48% (67/141) |
| Succinylcholine | 2% (6/320) | 17% (1/6) | 1% (2/320) | 50% (1/2) |
| Missing data | 1% (2/320) | 50% (1/2) | 2% (7/320) | 29% (2/7) |
| Intraoperative Variables Examined Before Tracheal Extubation | | | | |
| Clinical criteria | 49% (156/320) | 44% (69/156) | 45% (142/320) | 30% (42/142) |
| Pharmacological reversal | 26% (83/320) | 36% (30/83) | 25% (81/320) | 44% (36/81) |
| NMT monitoring | 12% (37/320) | 62% (23/37) | 11% (34/320) | 29% (10/34) |
| Combinations of clinical tests/ pharmacological reversal/ NMT monitoring | 11% (36/320) | 50% (18/36) | 18% (59/320) | 32% (19/59) |
| Missing data | 2% (8/320) | 12% (1/8) | 1% (4/320) | 0% (0/4) |
| Tympanic temperature at arrival in the PACU | | | | |
| Temperature <36°C | 46% (146/320) | 34% (49/146) | 70% (223/320) | 43% (97/223) |

NMBD = neuromuscular blocking drug, TOF = train-of-four, NMT = neuromuscular transmission. PACU = postanesthetic care unit. The clinical criteria were those used in daily practise, at the discretion of the individual anesthesiologist.

Cammu G, et al. Anesth Analg 2006; 102: 426-9.

# The Clinical Benefits of Routine Monitoring and Reversal[1]

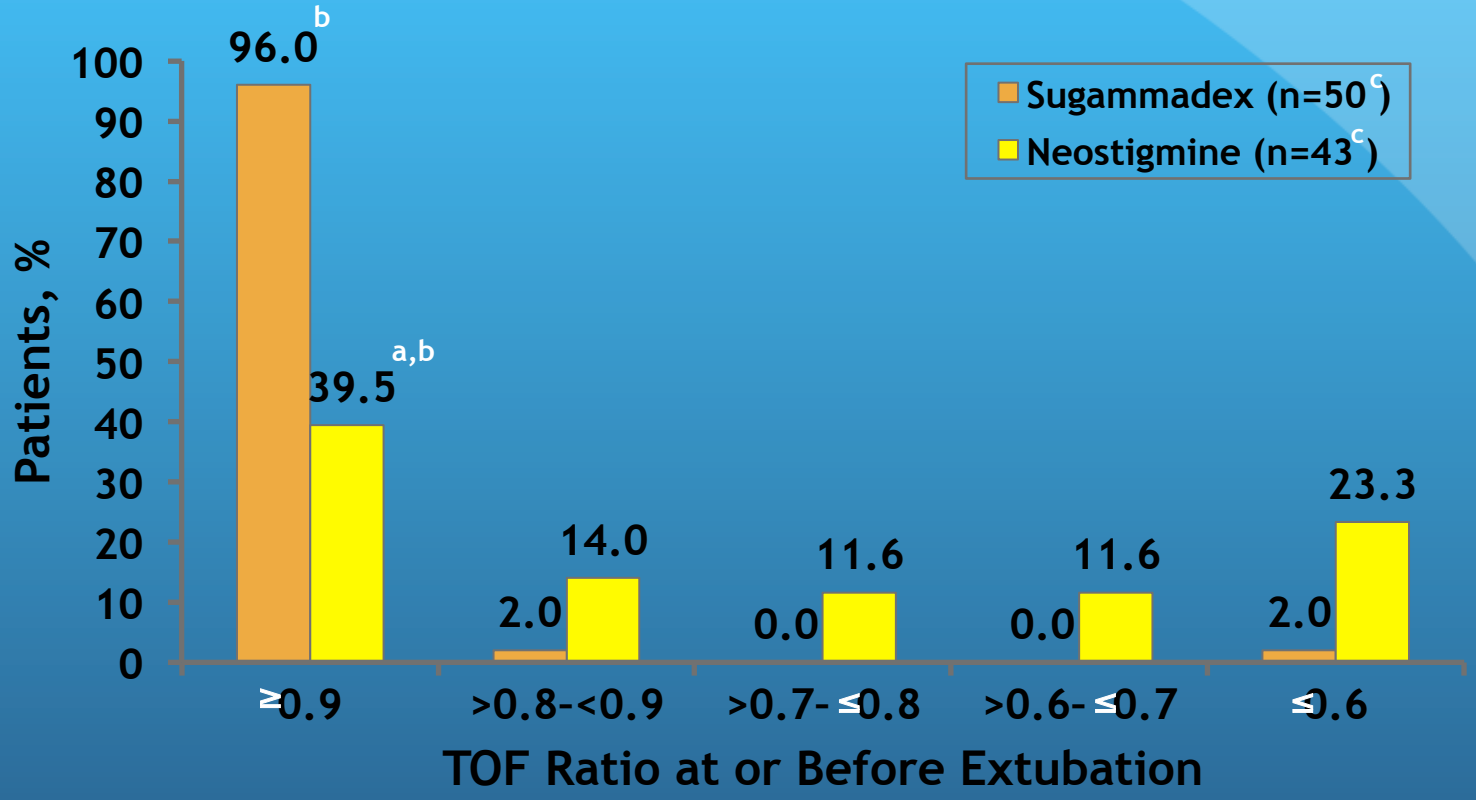



NMB=neuromuscular blockade; TOF=train of four.



1. Baillard C et al. *Br J Anaesth*. 2005;95:622-626.

# Sugammadex Increases Likelihood that Extubation Occurs at TOF ≥0.9[1]




[a] *P*<0.0001 for sugammadex vs neostigmine (Fisher's exact test).
[b] Includes 7 patients in the sugammadex group and 5 patients in the neostigmine group in whom the monitor was switched off before extubation because the patient was already awake or moving but who had reached a train-of-four (TOF) ratio of ≥0.9.
[c] Patients with data available: In total, 3 patients (1 sugammadex and 2 neostigmine) were excluded from the figure because monitoring was stopped before extubation, as the patient moved or woke up. In addition, 1 neostigmine patient was not included because the TOF trace was considered to be unreliable.



1. Sabo et al. *J Anesthe Clinic Res.* 2011;2:1-7.

# Overview best practice

- When are NMB needed and to what depth?
- Induction dose
  - Succinylcholine versus rocuronium
- Maintenance dose
  - Bolus versus infusion
- NMB monitoring
  - TOF  PTC
- Reversal
  - Tof 90 % needed
  - Predicatable reversal

# You need to monitor NMT to avoid PORC How do you measure NM block?

1. I give the appropriate NMB dose and assume to be deep enough.
2. I ask the surgeon if he is happy and so will I
3. I measure the single twitch or TOF on one muscle till no answer and assume that all muscles are relaxed.

This is all wrong and might lead to insufficient NMB


Kopman A.F. Anesthesiology. 1984;61:83-5

# NMB effect on adductor pollicis vs other muscles

1. At induction last to relax OKE
2. During surgery most sensitive Not OKE
3. Last to recover at end surgery OKE

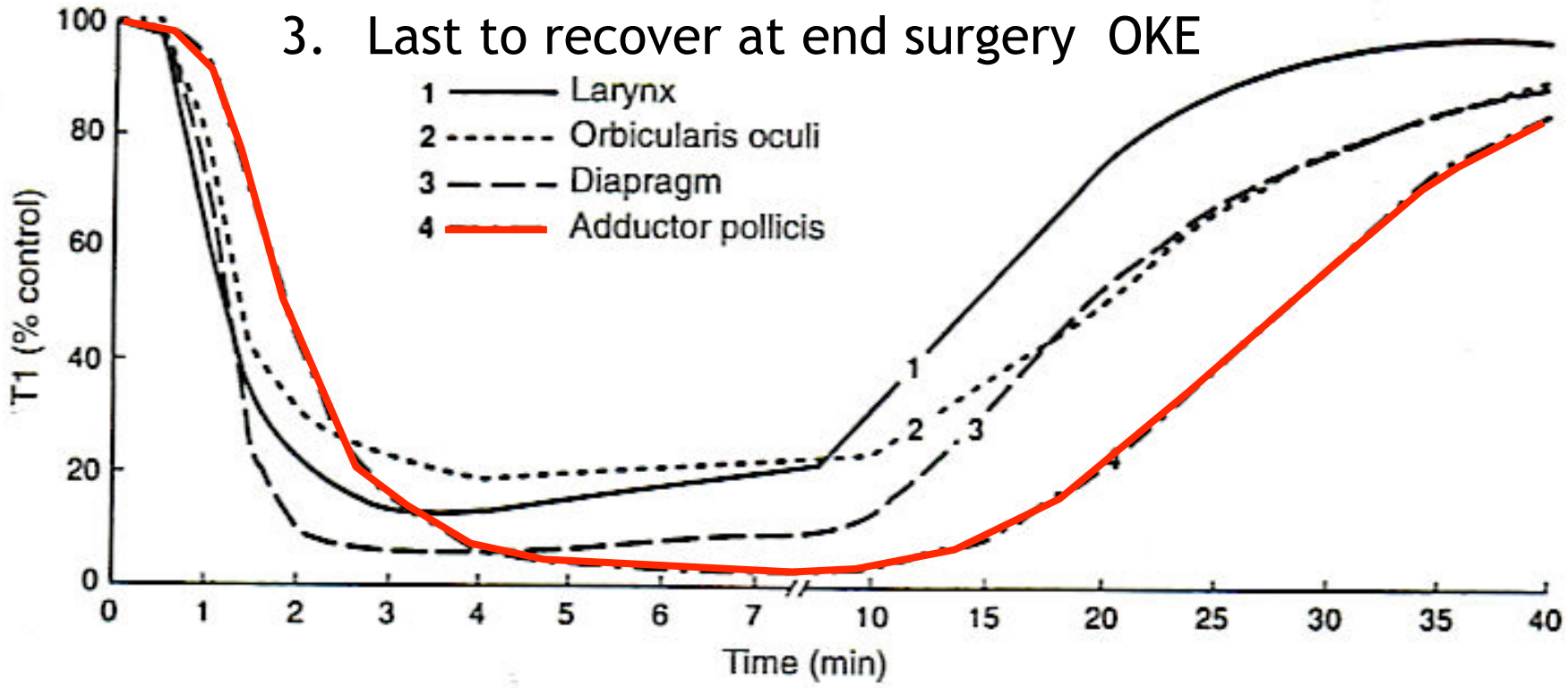
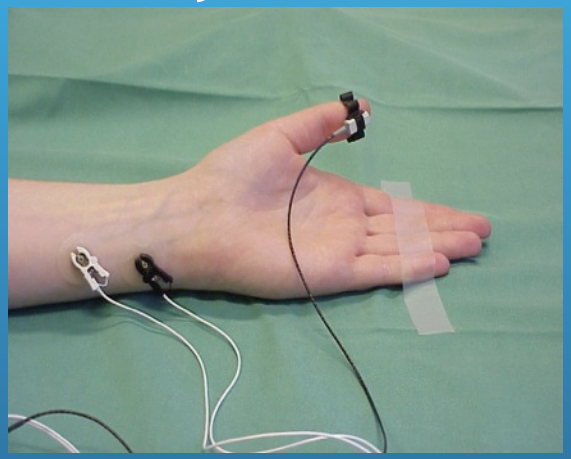
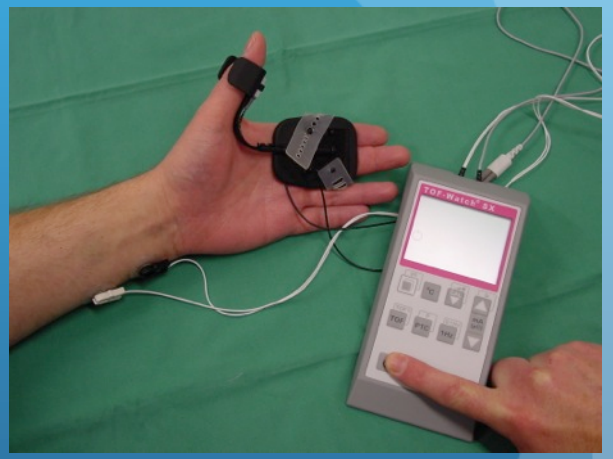
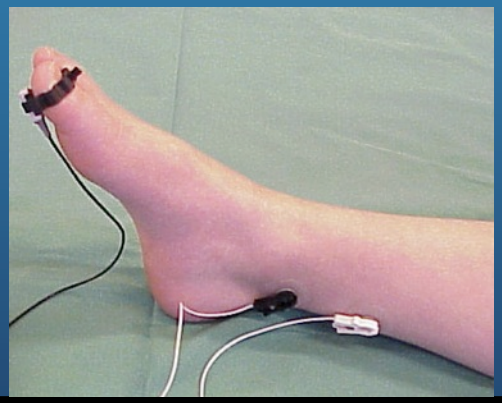
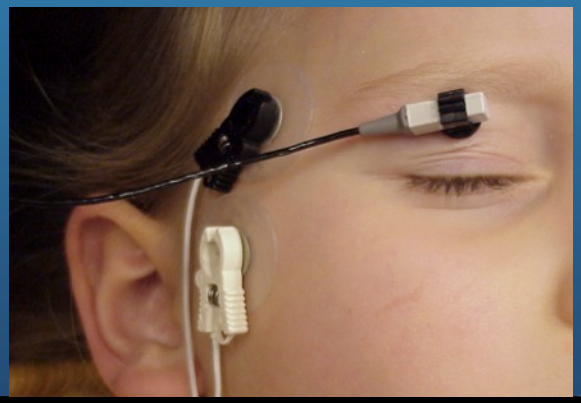


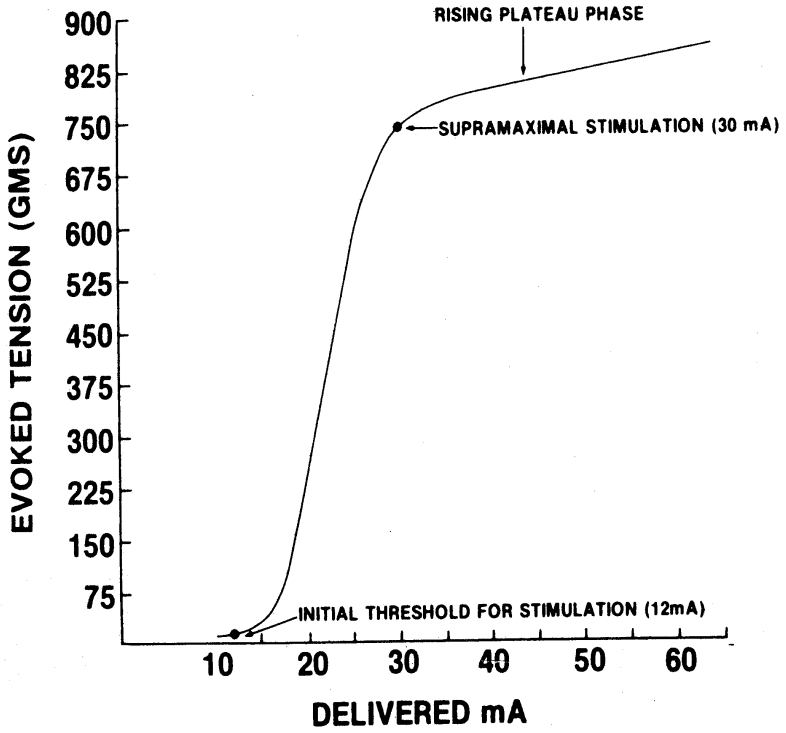

Fig. 21.4 Onset and recovery of neuromuscular blockade after injection of vecuronium 0.07 mg/kg at four muscles. (Data from Donati *et al*. 1990, 1991.)

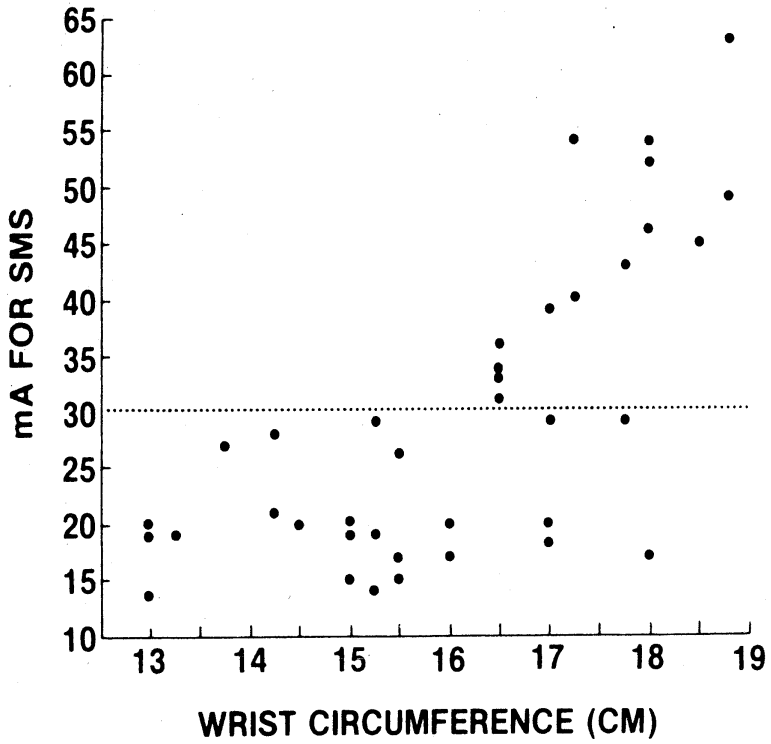
# Nerve stimulation and muscle acceleration

1. N ulnaris -> Adductor pollicis
2. N tibialis ->
3. N orbicularis -> eyelid or


# Why Supramaximal stimulation?



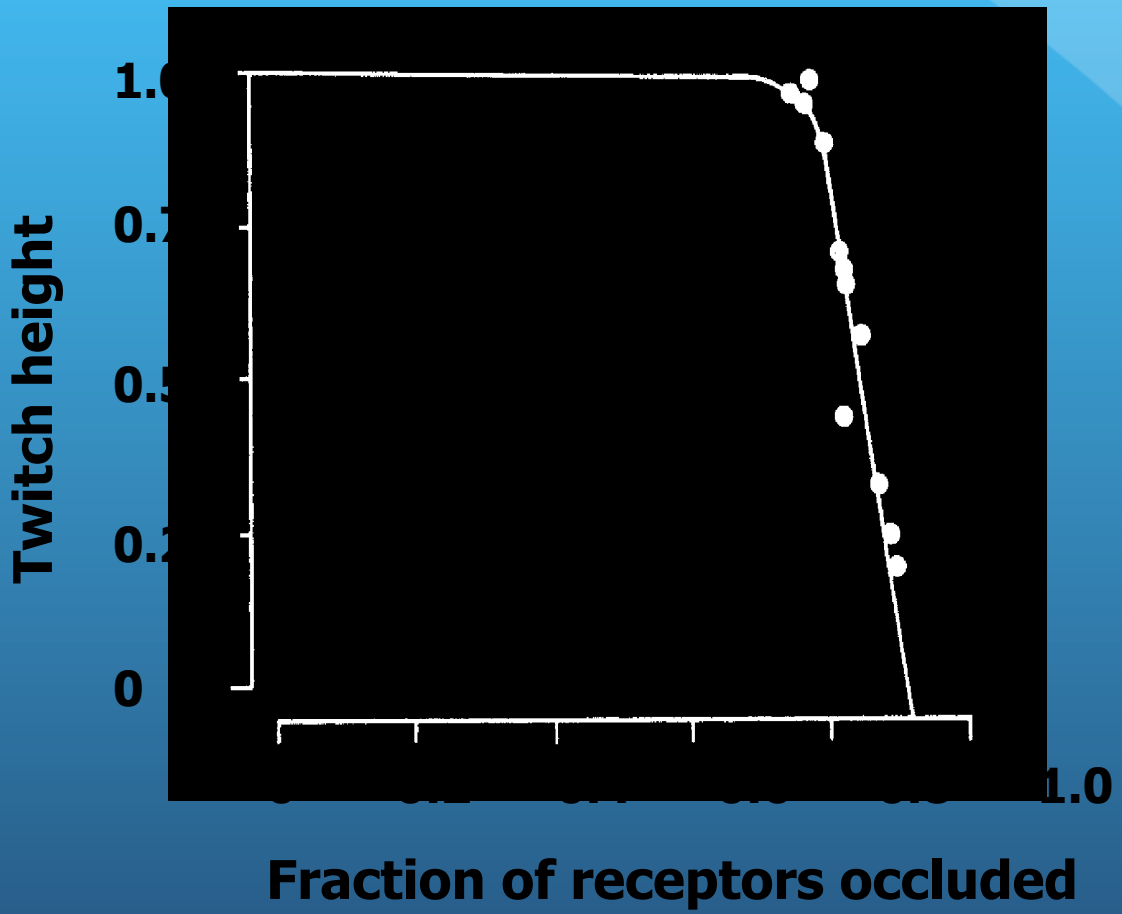




Kopman A.F.,Anesthesiology, 1984;61:83-5

# Troubles in monitoring

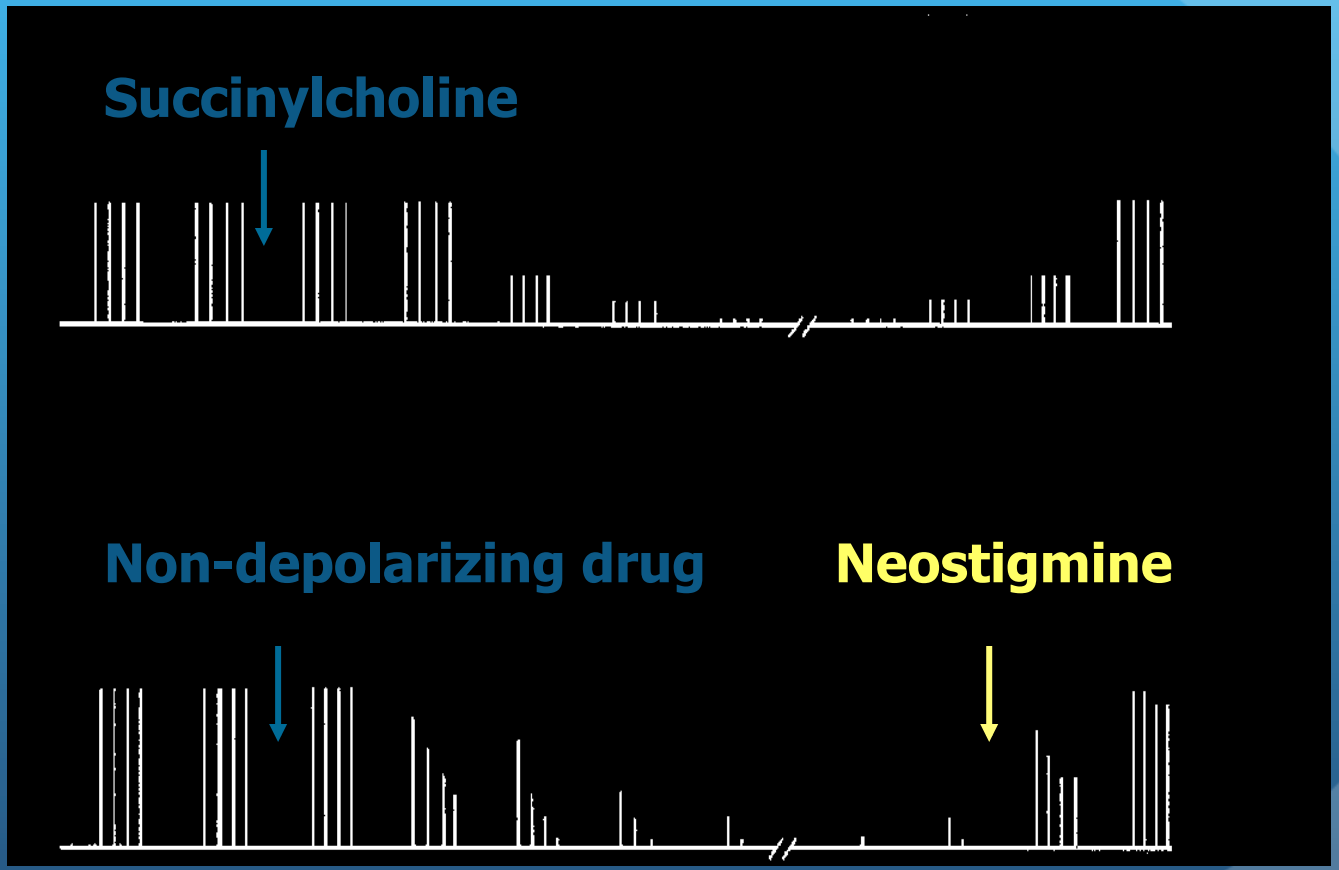
1. Electrodes not correct position
    1. To close to adductor muscle. Always TOF 4 through direct muscle stimulation
    2. Two electrodes to close: no current through depth
    3. Two electrodes to far: current too broad
    4. Two electrodes not over nervus: no stimulation
2. Electrodes quality
    1. Electrodes dried out: no electrical current
3. Thumb
    1. Not free movable
    2. No preload or no resistance
4. Cold muscle, bad perfusion

# Receptor occupation and twitch height




*From Stoelting: Pharmacology & physiology in anesthetic practice*

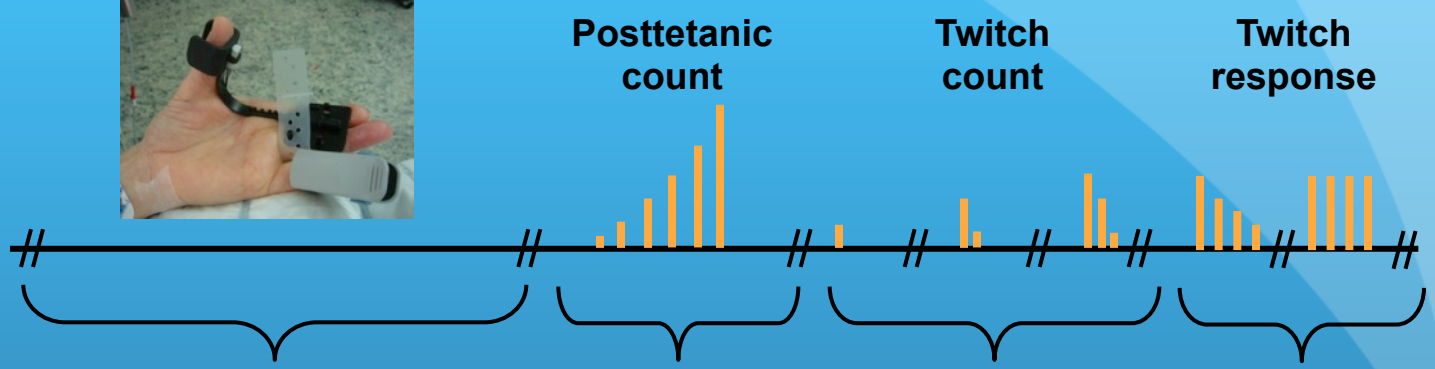
# TOF: depol – niet-depol




*Hunter, N Engl J Med 1996, 332*

# Various Depths of NM Blockade

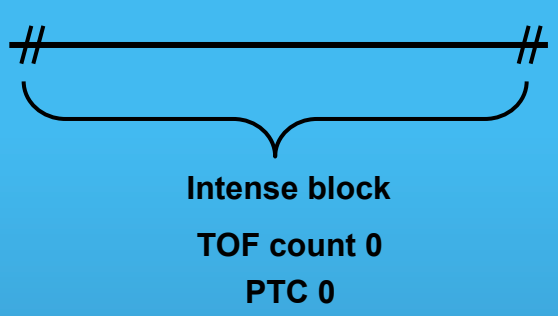





| Level of block | Intense block | Deep block | Moderate block | Superficial block |
|---|---|---|---|---|
| Response to TOF | TOF count 0 | TOF count 0 | TOF count 1-3 | TOF count 4 |
| Response to PTC | PTC 0 | PTC ≥1 | PTC ≥20 | T4 / T1 % |

- Intense blockade: no response to either TOF or PTC stimulation
- Deep blockade: response to PTC but not to TOF stimulation
- Moderate blockade: reappearance of response to TOF stimulation
- Superficial blockade: T4 response divided by T1 response

PTC, posttetanic count; TOF, train-of-four.



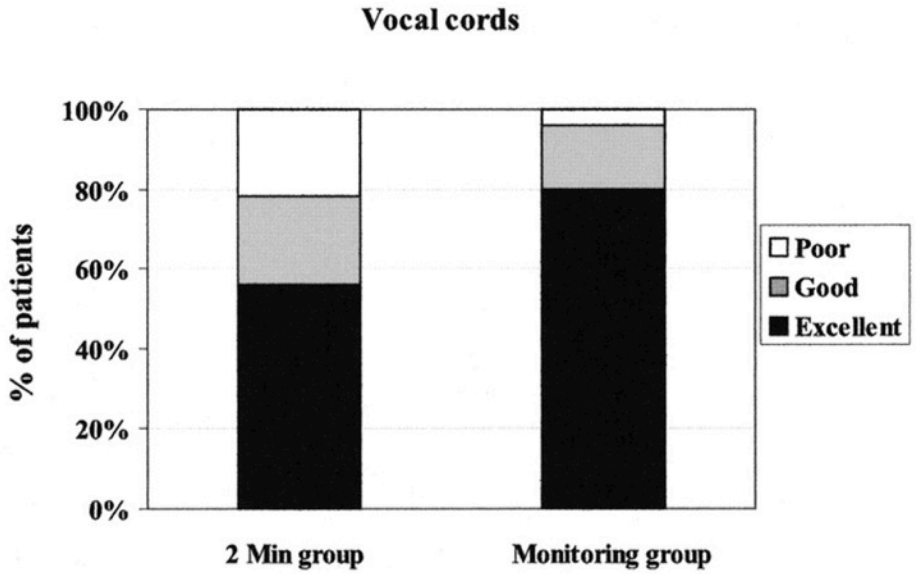

# Intense block is needed …

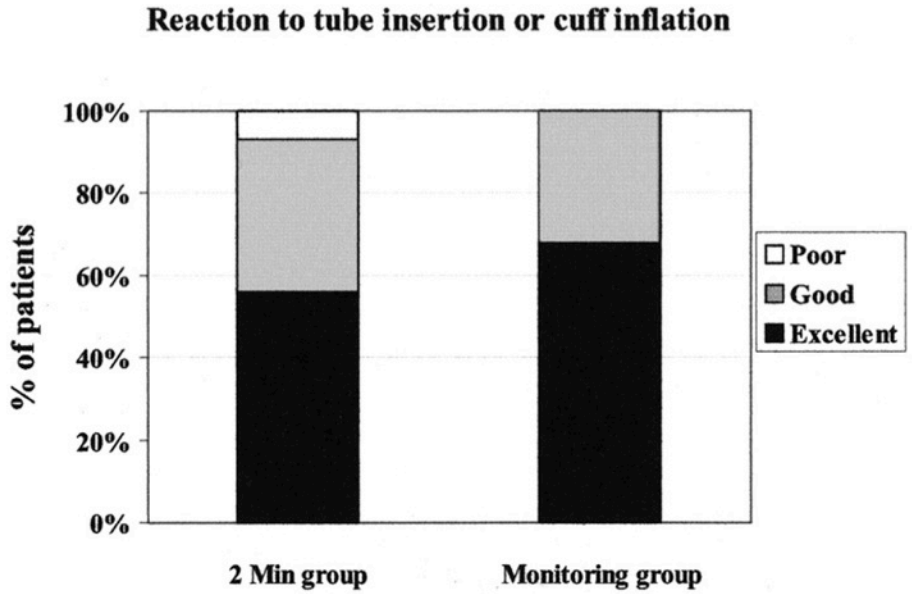
- During endotracheal intubation
  - Vocal cords are most resistant
  - Very high dose of NMB to reach this very fast during RSI
- Laser-surgery on vocal cords
  - Continuous infusion of succinylcholine -> rocuronium & suggammadex
- But I can intubate without NMB ! ! !
  - High dose Sevoflurane-Remifentanyl-Propofol or awake !
  - Yes … but not ideal in most patients…

# Intubation without NMB is possible but most studies do not compare with NMB.

- Fotopoulou G Fundam Clin Pharmacol. 2012;26:72. **Management of the airway without the use of neuromuscular blocking agents:**
  - Remifentanil combined either with propofol or with inhaled anesthetic agents has been proved to provide acceptable intubating conditions
  - Anesthesiologists must be conscious with the use of remifentanil
- Demirkaya M J Clin Anesth. 2012;24:392. **The optimal dose of remifentanil for acceptable intubating conditions during propofol induction without neuromuscular blockade.**
- Erhan E Eur J Anaesthesiol. 2003;20:37 **Tracheal intubation without muscle relaxants: remifentanil or alfentanil in combination with propofol.**
  - intubating conditions were significantly better in patients who received remifentanil 4 microg kg(-1) compared with those who received alfentanil 40 microg kg(-1) or remifentanil 2 microg kg(-1).

# Intubating conditions are better with deep NMB according to the vocal cords and reaction to tube insertion

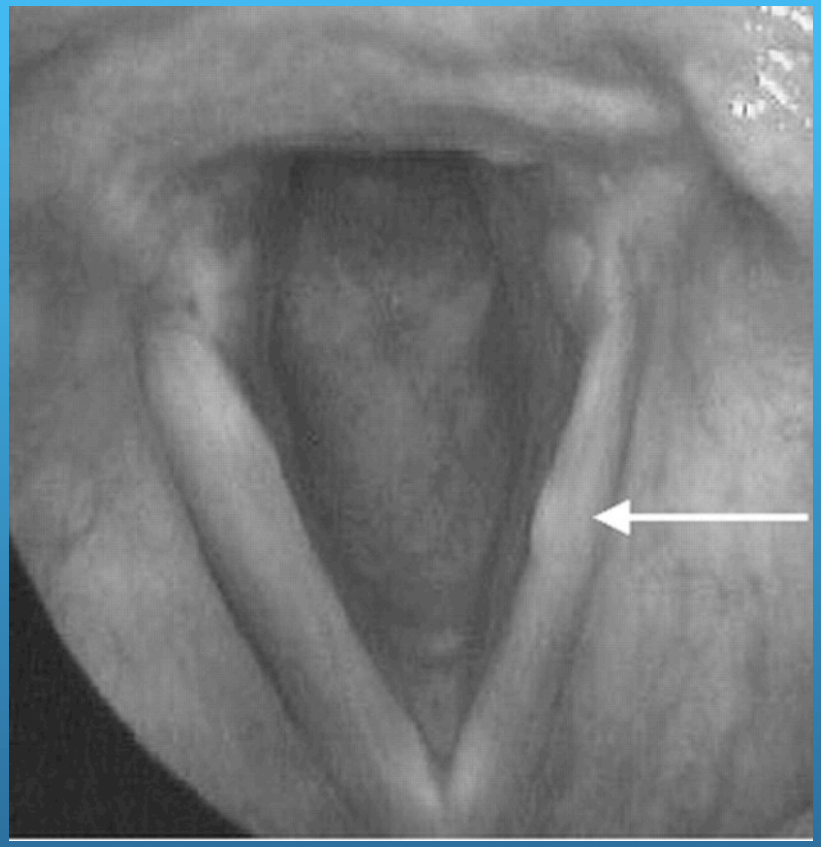


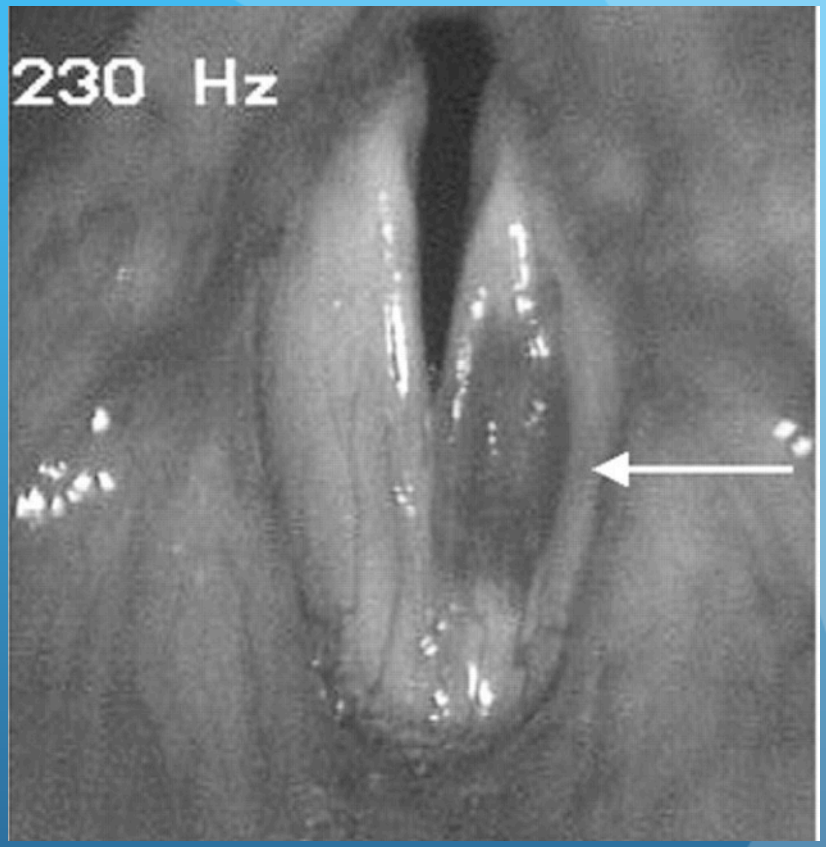

**2-Min group = Tracheal intubation 2 min after administration of atracurium; monitoring group = Tracheal intubation at maximum block.**

**Mencke T et al.** Does the Timing of Tracheal Intubation Based on Neuromuscular Monitoring Decrease Laryngeal Injury? A Randomized, Prospective, Controlled Trial **Anesth Analg 2006;102:306-312**

# Superficial NMB has more complications

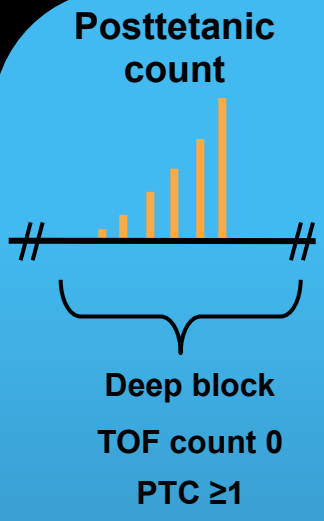


Thickening of the left vocal fold (localized swelling of the mucosa) at 24 h after surgery




Hematoma (caused by bleeding into a vocal cord) of the left vocal cord at 24 h after surgery.

Mencke T et al. Anesth Analg 2006;102:306-312




# Deep block is needed…

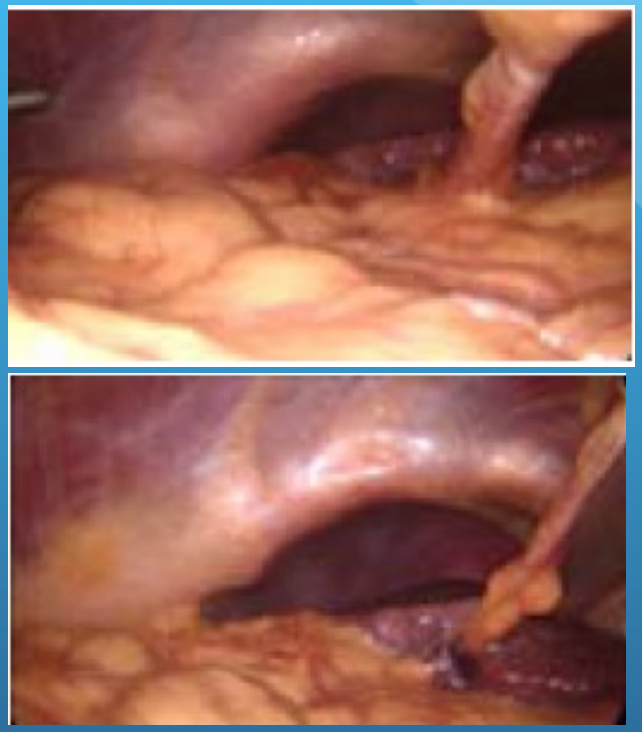
- Laparoscopy
  - Diaphragm is more resistant than thumb
- Laparotomy
  - Abdominal muscles are more resistant than thumb
- Neurosurgery with fixated head,…
  - Smal movements can be deadly
- But I can do this without NMB ! ! !
  - Deep anesthesia with inhalation or remifentanyl.
  - Yes but…not ideal in most patients.

# I can do laparoscopy without NMB but…

- The effects of NMB on peak airway pressure and abdominal elastance during pneumoperitoneum.
  - Chassard D Anesth Analg 1996; 82: 525
  - *Pigs have a non linear behaviour different from humans*
  - *Elastance is not changing either in humans*
- Gynecologic laparoscopy with or without curare?
  - Chassard D Ann Fr Anesth Reanim 1996; 15: 1013
  - *Surgeon was asked if he could work. Additional dose is given if he could not work*
- A comparison of the effect of two anaesthetic techniques on surgical conditions during gynaecological laparoscopy
  - Williams MT. Anaesthesia. 2003; 58: 574
    - *Without curare shorter operation, higher PVO, trocar placement difficult.*
- No supplemental muscle relaxants are required during propofol and remifentanil total intravenous anesthesia for laparoscopic pelvic surgery.
  - Peak CM J laparoendosc Adv Surg Tech 2009; 19: 33
    - *Effect is not measured .*

# Decreased Level of Insufflation Pressure With NMB-Induced Relaxation[1]

- NMB-induced relaxation maintained the integrity of pneumoperitoneum without increased $CO_2$ insufflation pressure



**Visual field during a laparoscopic procedure approaching recovery from NMB (top) and deep NMB (bottom).**

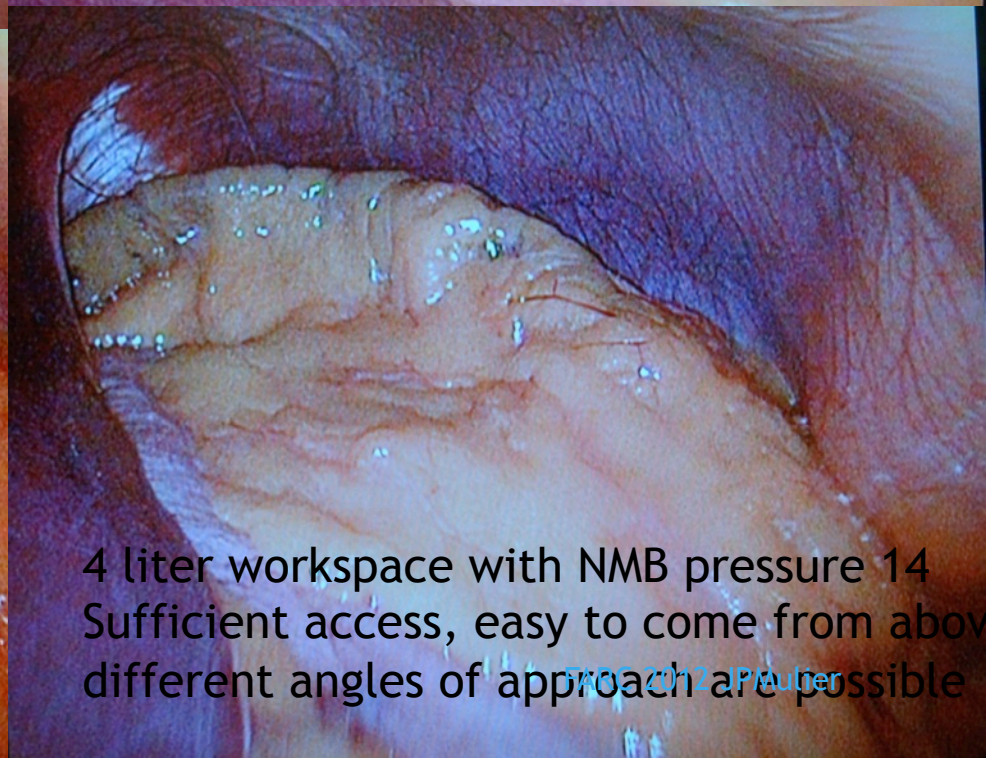
NMB=neuromuscular blockade; $CO_2$=carbon dioxide.

**1.** Chui PT et al. *Anaesth Intensive Care*. 1993;21(2):163-171.

1 liter workspace no NMB pressure 11
Not sufficient no access to upper abdomen

2 liter workspace no NMB pressure 13
Ceiling is higher but still not enough acces
from every incidence

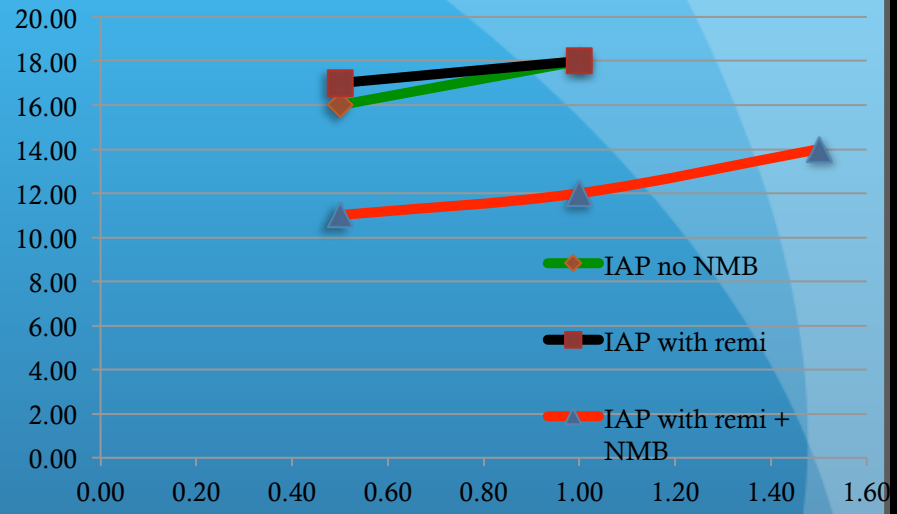
3 liter workspace no NMB pressure 15
Sufficient access for upper abdomen



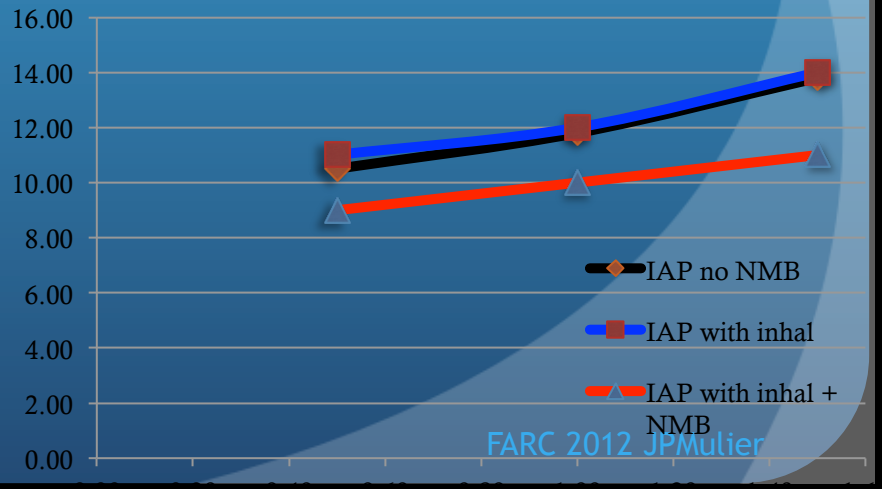
4 liter workspace with NMB pressure 14
Sufficient access, easy to come from abov
different angles of approach are possible

# Effect of TIVA & 1 MAC Desflurane

- Prop anesthesia
  - + Remifentanyl
  - + Remifentanyl and Rocuronium

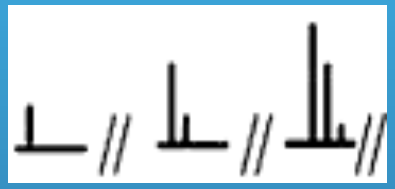


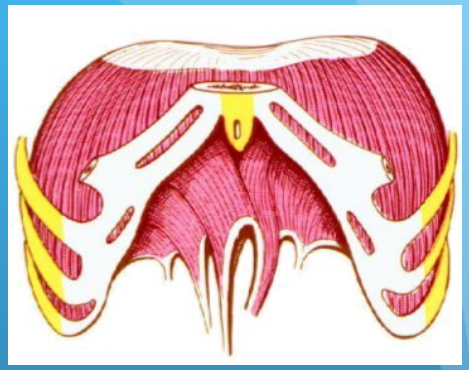

- Propofol anesthesia
  - Replaced by Desflurane
  - Desflurane + Rocuronium



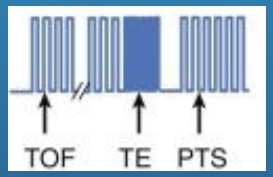
# Deep block in abductor pollicis means moderate block in abdominal muscles and diaphragm

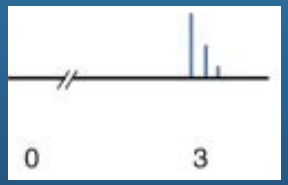
**Shadow block**

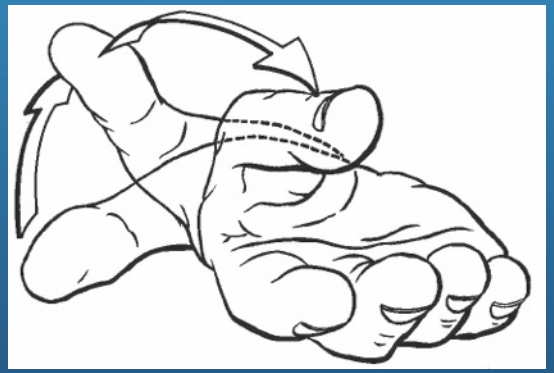


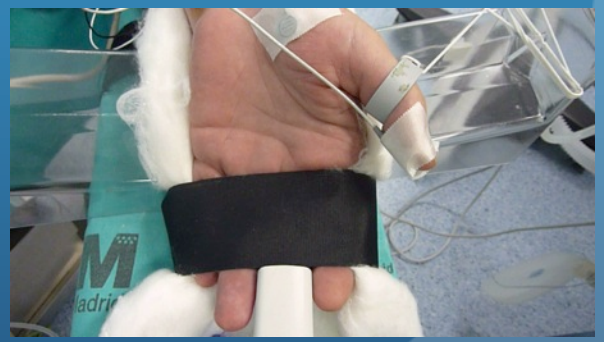


**Deep block**

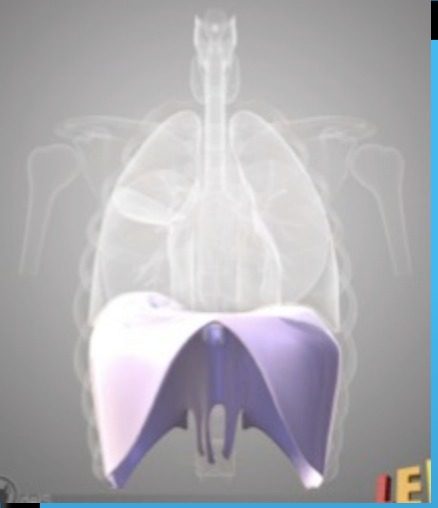


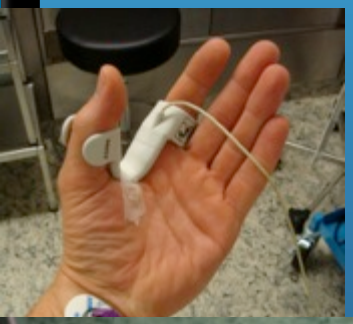


**10 PTCs**



# Difference Between Diaphragm and Adductor Pollicis

- Monitoring of the peripheral muscles often overestimates the degree of diaphragmatic relaxation, but is a safe predictor of recovery.
  - Moerer O. *Anasthesiol Intensivmed Notfallmed Schmerzther*. 2005;40:217



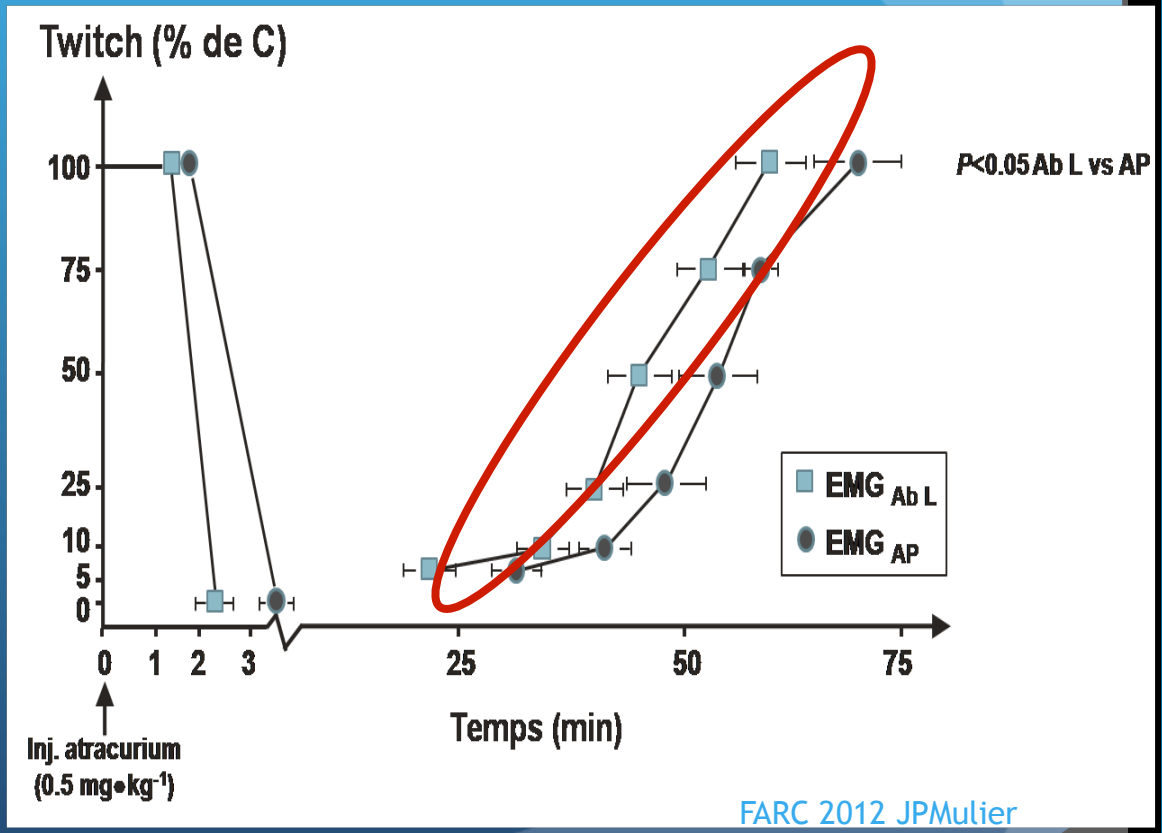
- The diaphragm is more resistant than the adductor pollicis to rocuronium and has a faster recovery of the twitch height.
  - Cantineau JP *Anesthesiology*. 1994;81:585

# Time difference when bolus NMB given between abdomen – adductor pollices

**Sensibilité à l'atracurium des muscles abdominaux latéraux***

K. Kirov, C. Motamed, X. Combes, P. Duvaldestin, G. Dhonneur**

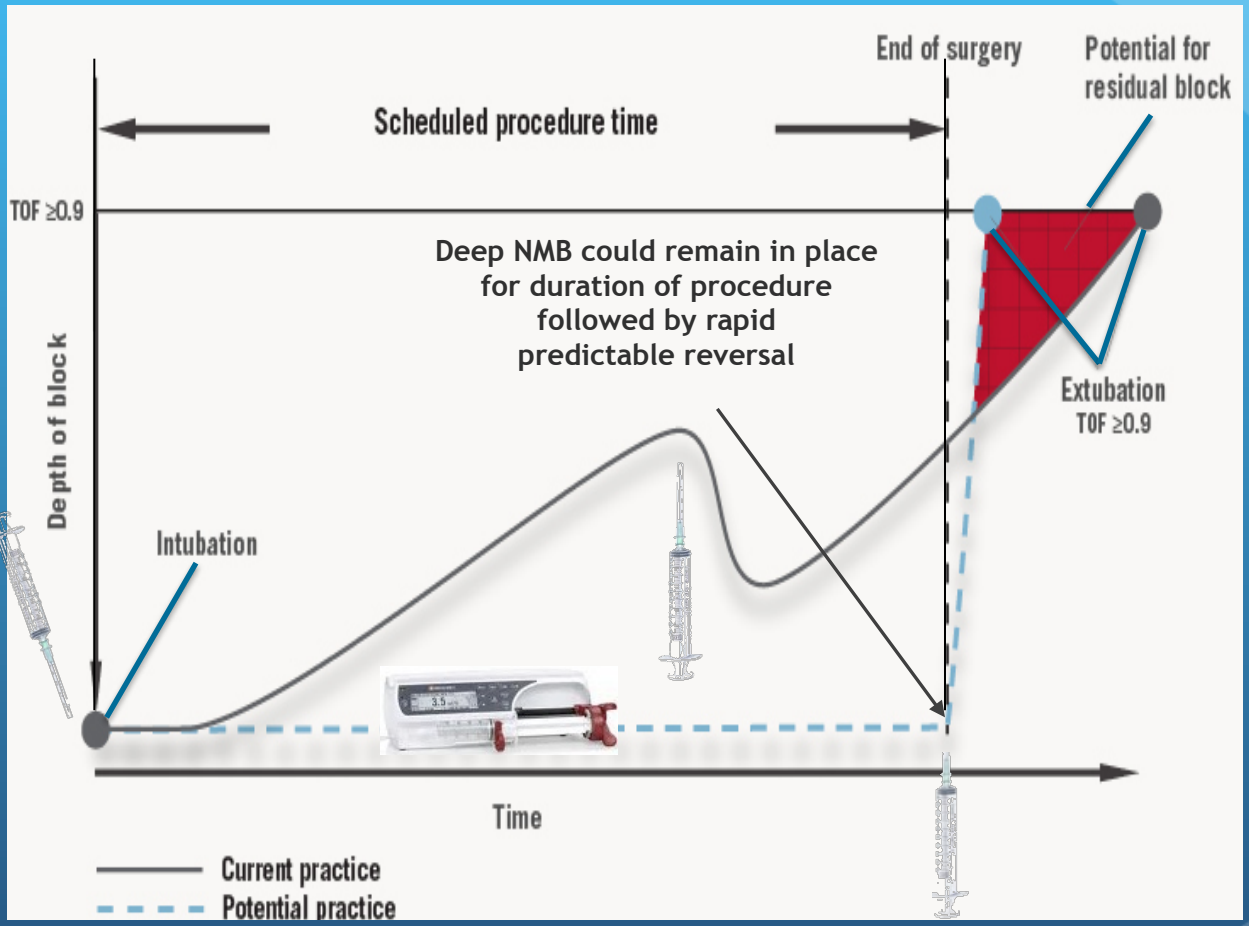
**Sensibility to atracurium of the lateral abdominal muscles**
**Objective:** To study the effect of atracurium on the electromyographic activity of the lateral abdominal muscles and adductor pollicis in anaesthetized subjects.




**Lateral abdominal muscles blockade have a faster onset and recovery than adductor pollices**

Kirov K et al. *Ann Fr Anesth Reanim.* 2000;19:734–738.

# Solution to Both Problems: Continuous Infusion to a Deep Block



# The Benefits of Deep Neuromuscular Blockade: Surgical Procedure

**Low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy (Review)**

Gurusamy KS, Samraj K, Davidson BR

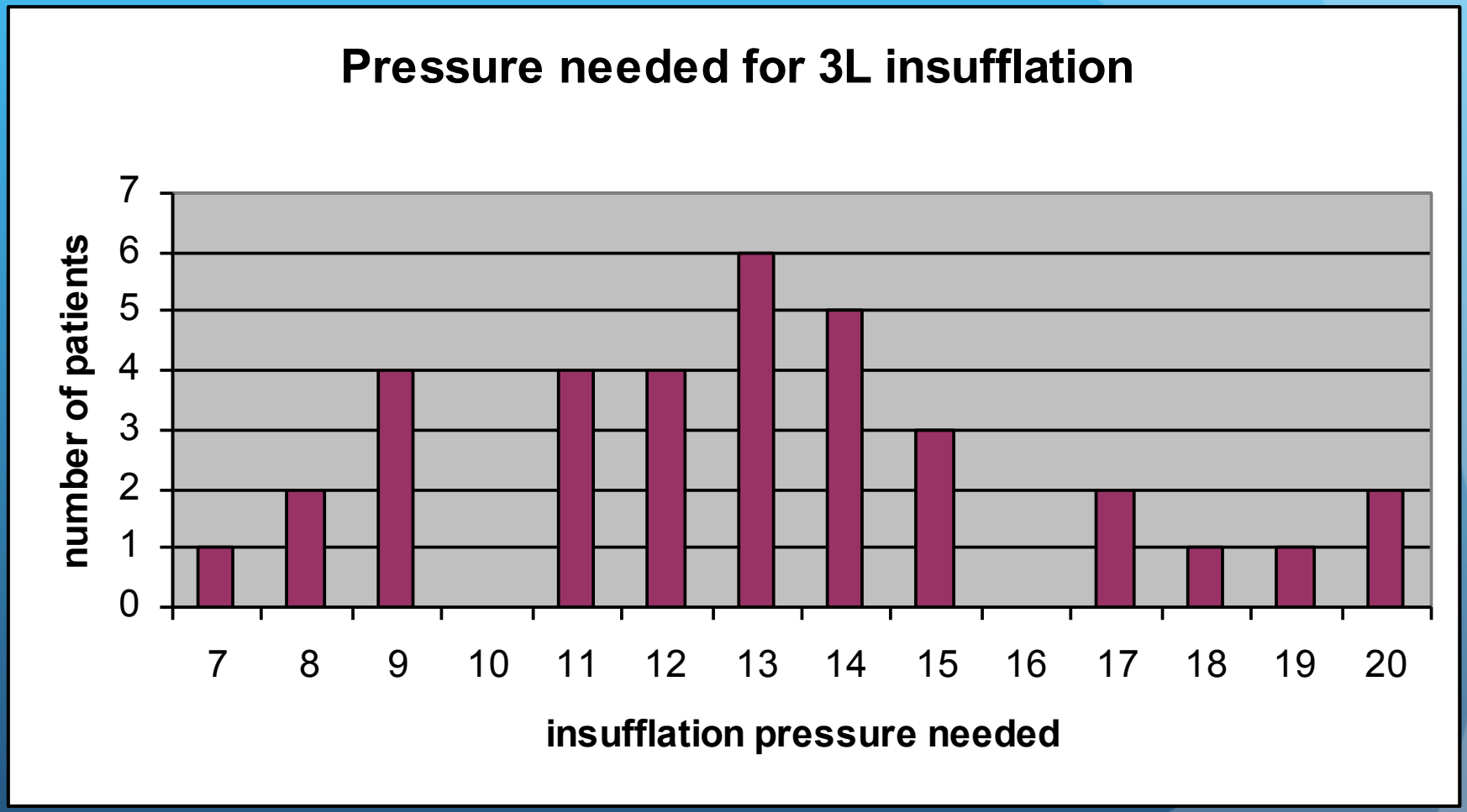
- Authors' conclusions
  - Low pressure pneumoperitoneum appears effective in decreasing pain after laparoscopic cholecystectomy
  - The safety of low pressure pneumoperitoneum has to be established

Could NMBAs limit insufflation pressure?



Gurusamy KS, et al. Cochrane Database Syst Rev.

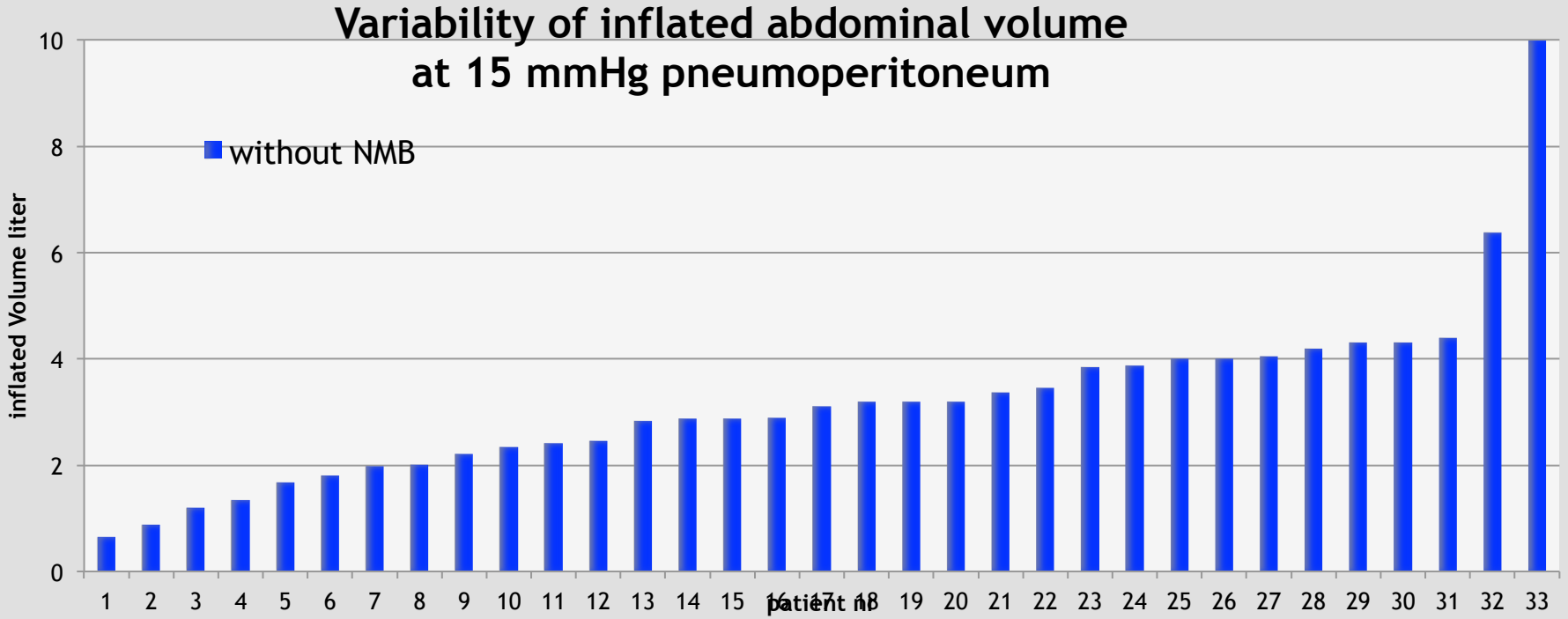
# We can choose the lowest IAP possible by using max NMB

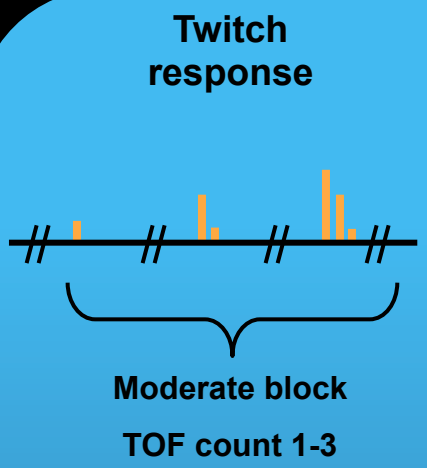



Mulier JP 2007

# Patient variability

- Inflated volume at 15 mmHg without NMB varies from 0,5 L to 10 L.
- Who needs NMB?
- Will the surgeon be comfortable?





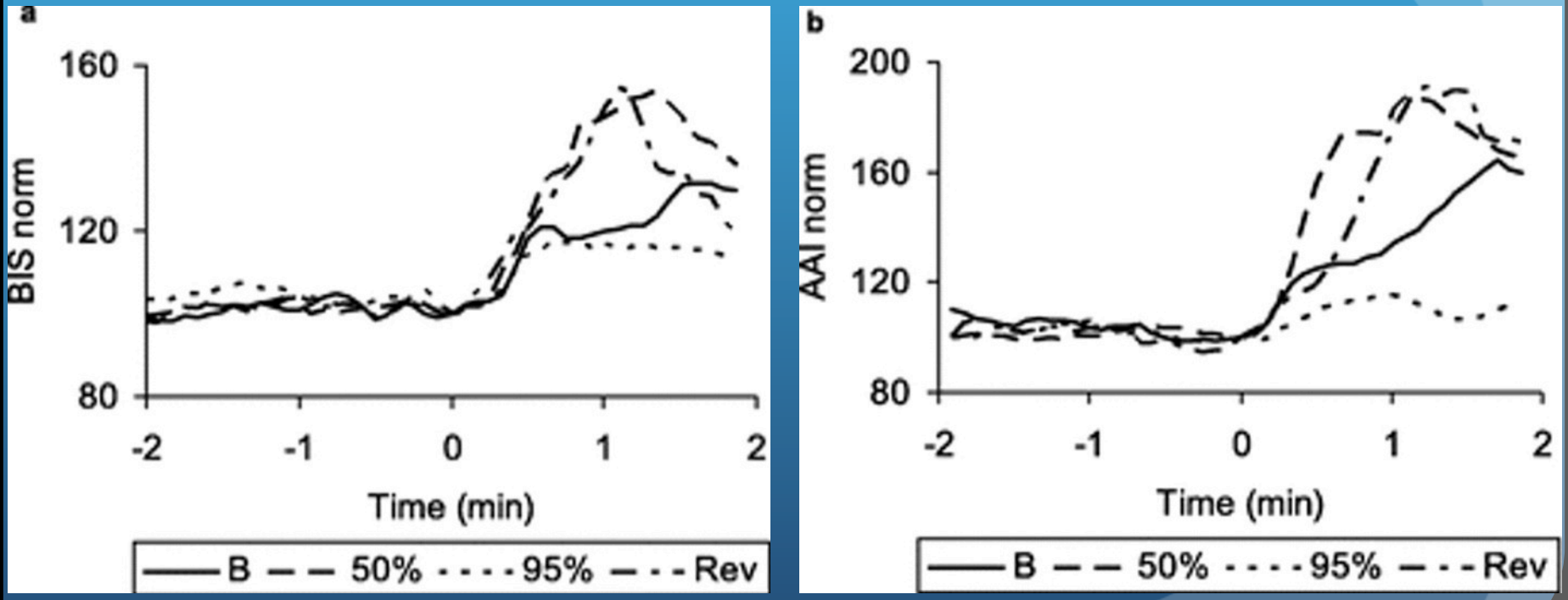

# Moderate block is needed…

- Facilitating ventilation
- Avoiding movements during surgery
- Reducing depth of anesthesia
- But I can do this without NMB
  - yes indeed
    - Use pressure support ventilation instead of NMB
  - But moderate block is still better than
    - Deep anesthesia with inhalation or remifentanyl.

# Low BIS should be avoided by use of NMB

- Low BIS relates to Hypotension; Peripheral hypoperfusion; Prolonged recovery times; Possible brain dysfunction

**BIS and auditory evoked potential index (AAI) 2 min before until 2 min after noxious tetanic stimulation at different degrees of NMB T1 depression in %**




Ekman A et al. Anesth Analg 2007;105:688-695

# With NMB no need for deep TIVA anymore?

- Opioid free anesthesia has many advantages.
- Inhalation anesthesia is easier to titrate and adapt
- Xenon will be the ideal inhalation agent in the future to combine with NMBA's.


XenoVent
allows to use
your ventilator
your safety alarms

to give Xenon in a closed circuit with less loss

# Deep NMB is needed

- When we have no space

1. Or the patient has a small abdomen to start
2. Or NMB is not very deep anymore at the diaphragm and abdominal wall
   - Even with TOF = 0 we can see sometimes movements
   - Intermittent bolus gives moments of insufficient NMB

# Do we need shorter acting NMB ? =How predictable are our surgeons?

- Do we punish our surgeon if he is speeding up?
- Do you like given extra bolus of a long acting NMB at the end of surgery because the last stich is retaken?
- Surgery time is shortening each year
  - More experience, less invasive, more lap
  - Better surgical equipment
  - Focused team work
  - Financial cost for the society if total surgery time is longer
- Non surgical time is easily > 1 h accounting for 50% of the time.

# Non-surgical time: last stitch till incision next patient

- Try to reach 30 minutes "Dexter"
- We reach less than 30 min average

| | Dr Dillemans | other |
|---|---|---|
| Av. Surgical time | 54 | 61 |
| Av. Non-surgical time | 12.5 | 20.1 |
| Complications rate | | |
| Mortality | 0.04% | 1.02% |
| Obstructions | 0.38% | 1.5% |
| Bleedings | 3.14% | 4.38% |
| Leakage | 0.17% | 2.7% |

- J&J analysis:

  RNY: 12,5 min ?

- Why is this possible?
  - ERAS (early recovery after surgery)
  - Short turnover: patient out and next patient into room
  - RAI Rapid anesthesia induction or use of induction room
  - SPT Short pre-incision surgical preparation time

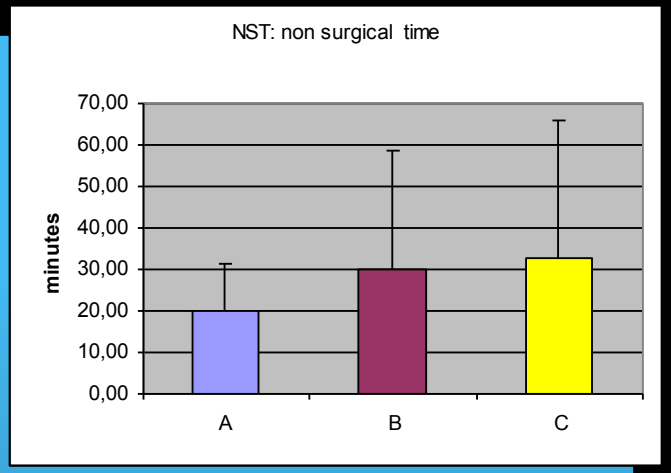
# Turn over time for all surgeries is very short

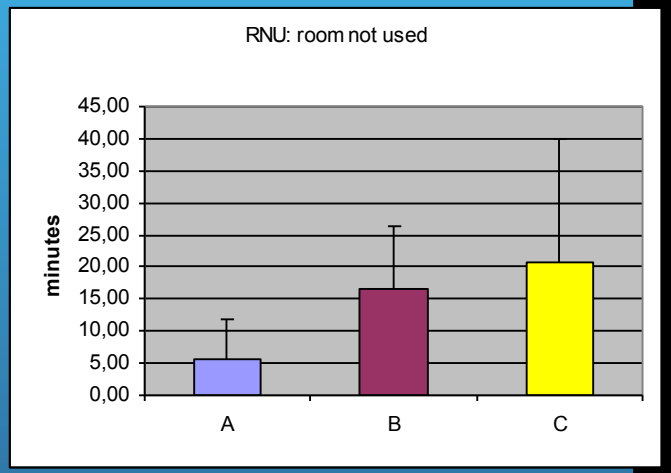
ASA 2008 JPMulier

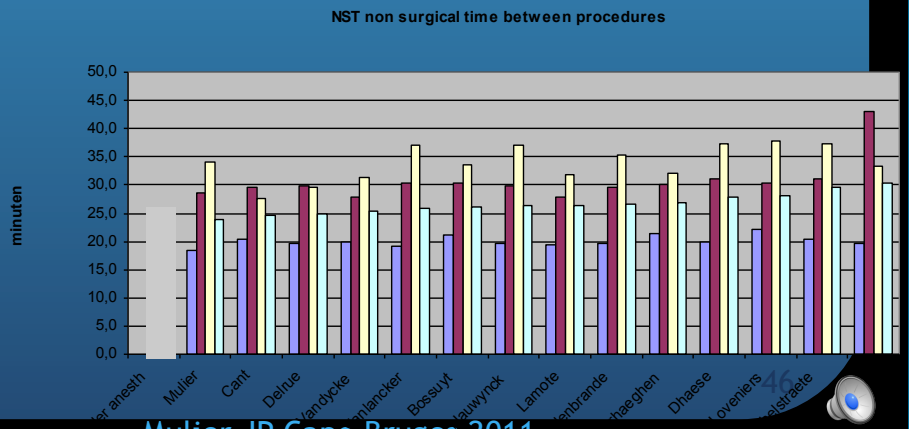
- A: induction next pat before awakening prev
- B: use pre induction room without anesthesia
- C: no use of pre induction room
- Multifactorial
  - Pre induction room?
  - Rapid awakening techniques
- Active management, supporting all team members to improve quality results in time gain!
  - Know what you do, simplify
  - Do it right from the first time

Non surgical time: 20 min

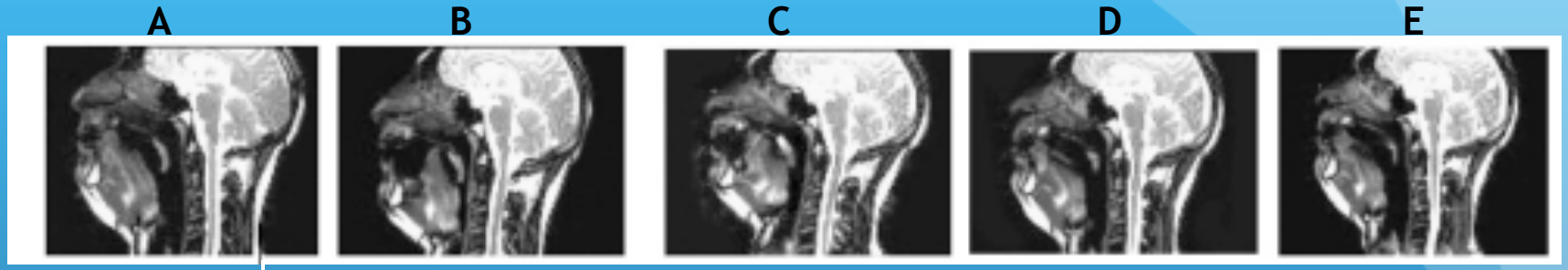
OP room not used: 6 min

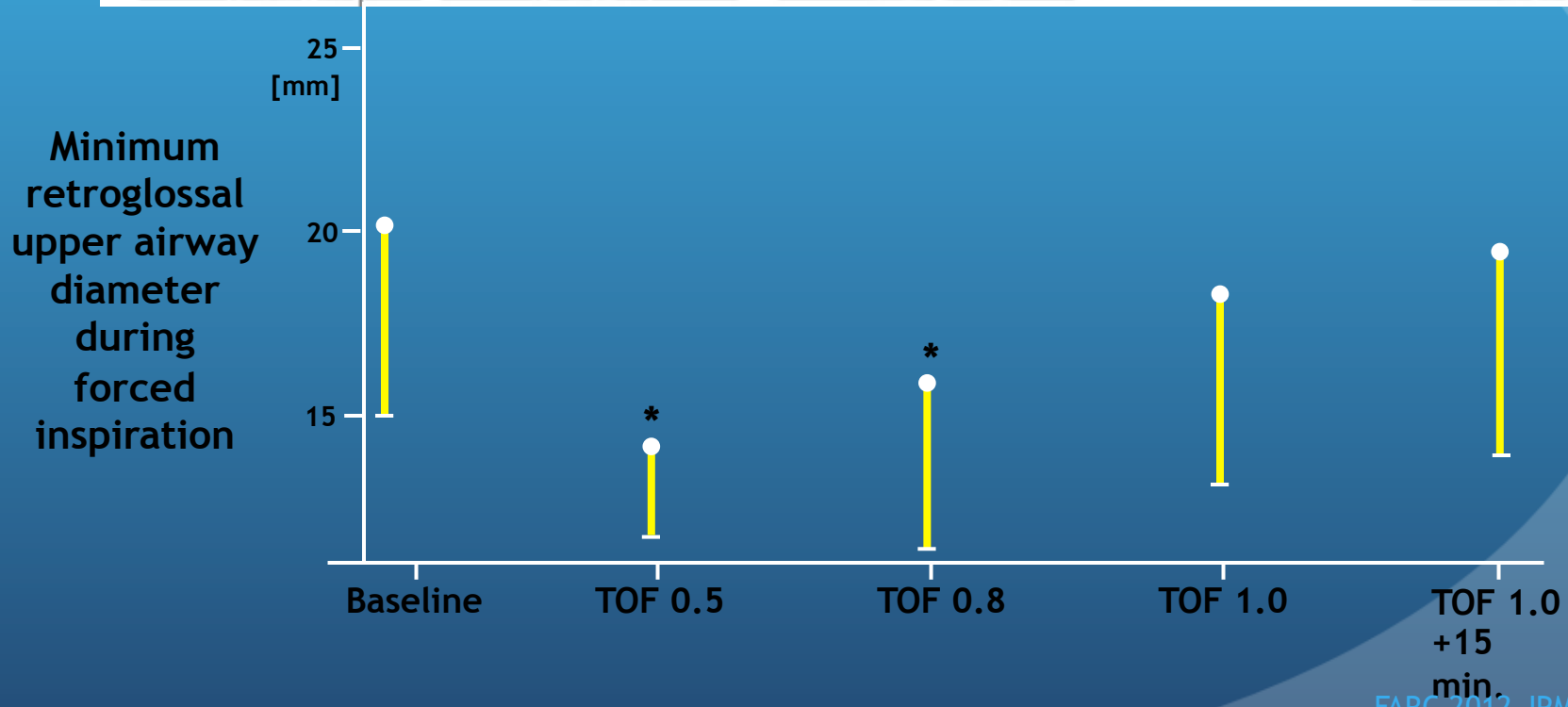


# Shorter acting NMB not enough! Full reversal needed!



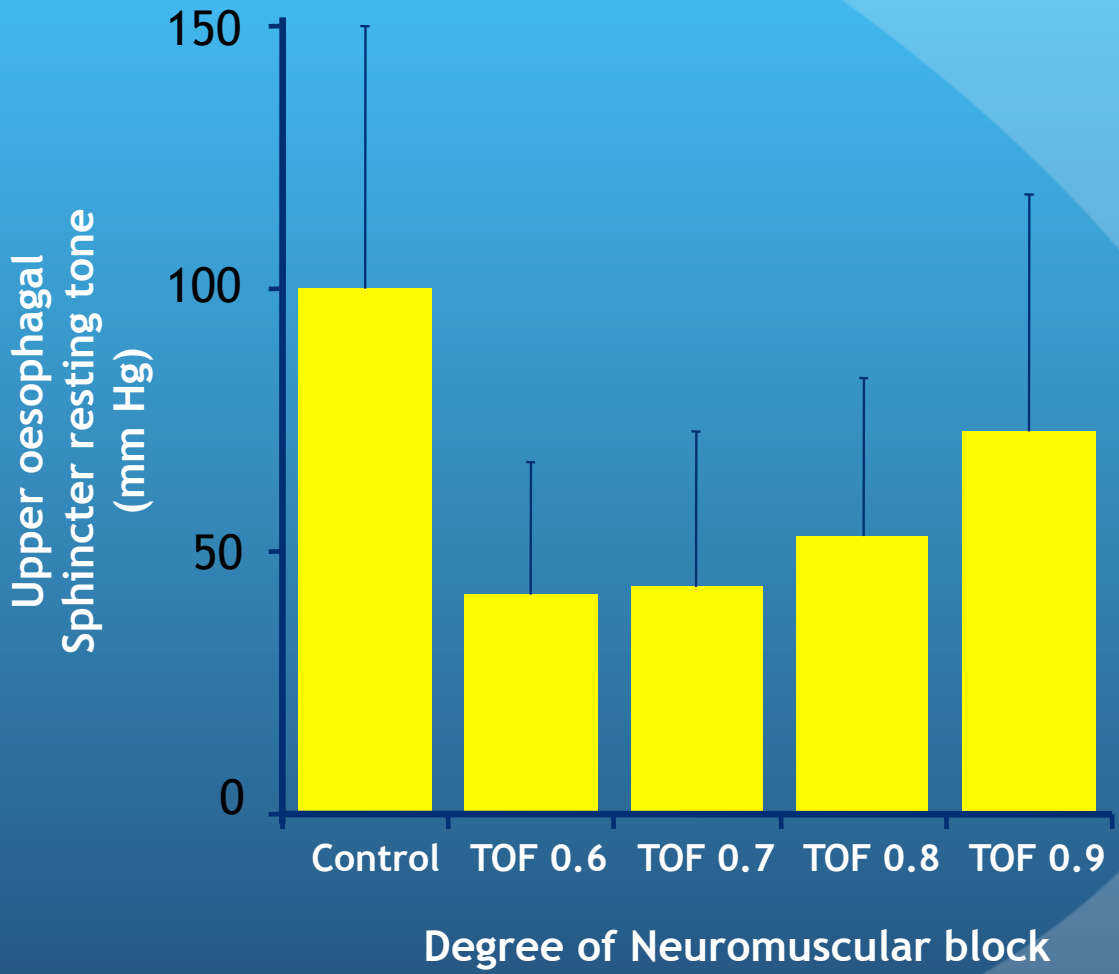



Eikermann, et al. *Am J Respir Crit Care Med* 2007;175:9-15

* *P*<0.05 versus baseline

# Pharynx Dysfunction Increases the Aspiration Risk

Human volunteers
Partially paralyzed

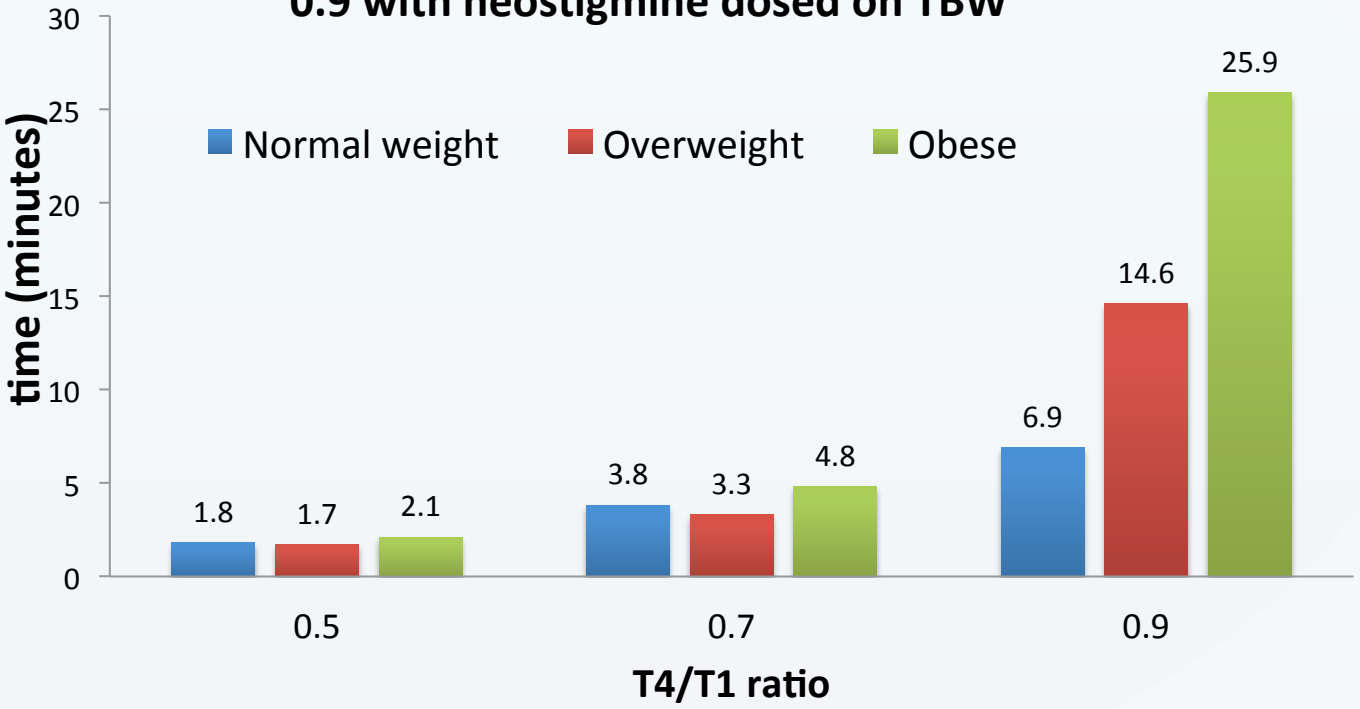





Eriksson LI, et al. *Anesthesiology*. 1997;87:1035

# Neostigmine is Less Effective and unpredicatable in Obese Patients

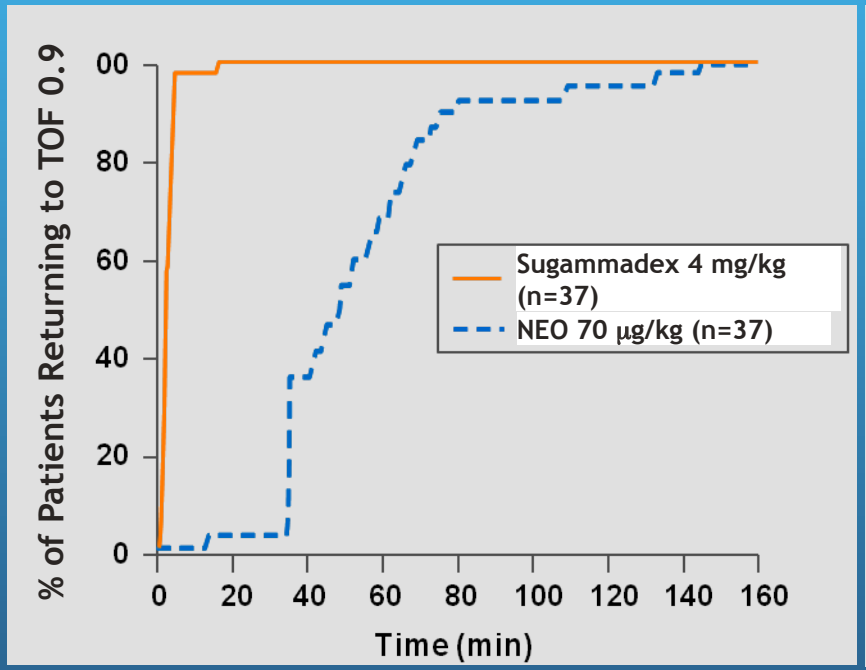
- Obese patients are more difficult to reverse with neostigmine.



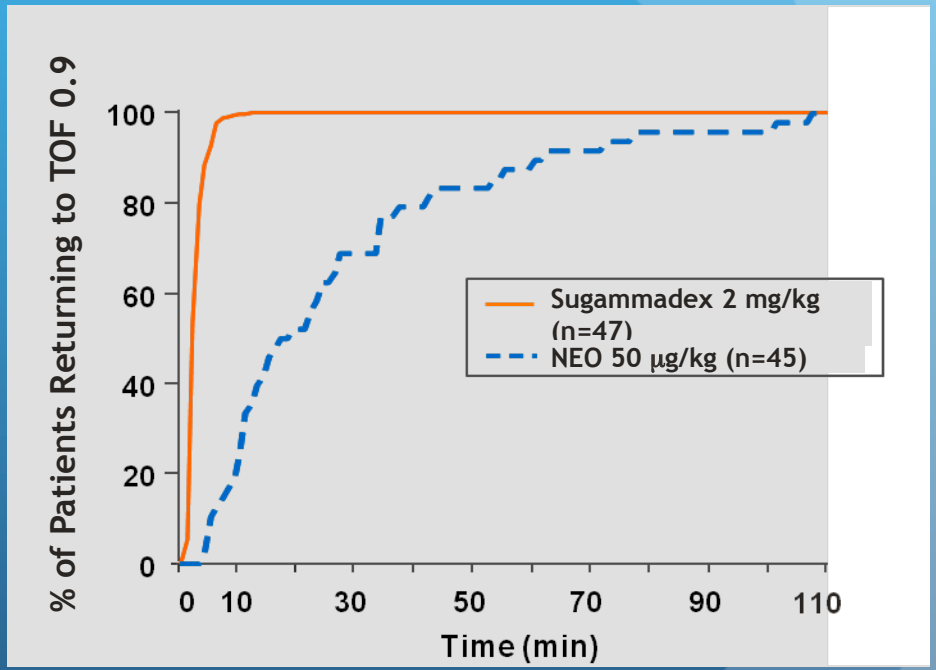

Suzuki T, et al. *Br J Anaesth*. 2006; 97 (2): 160-163.

# Predictability and Consistency of Sugammadex Reversal in Moderate and Deep NMB

**Reversal from 1 to 2 PTCs following rocuronium[1] 0.6 mg/kg**




**Reversal from T2 following rocuronium[2] 0.6 mg/kg**




NMB=neuromuscular blockade; PTCs=posttetanic counts; TOF=train of four; NEO=neostigmine.

1. Adapted from Jones RK et al. *Anesthesiology*. 2008;109:816–824. 2. Adapted from Blobner M et al. *Eur J Anaesthesiol*. 2010;27:874-881.

# Think what your surgeon needs to improve surgical outcome



- Principle of transdisciplinarity
- And for the surgeons:

‘Ask not only what the anaesthesiologist can do for you, ask also what you can do for the anaesthesiologist.’

*www.publicationslist.com/jan.mulier*