

*3<sup>rd</sup> International Symposium: Perioperative Care for Seniors  
June 4–6, 2015, Prague*

# *Muscle relaxation in seniors*

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Czech Republic*

*All diseases run into one, old age.*

*Ralph Waldo Emerson  
(1803 – 1882)*

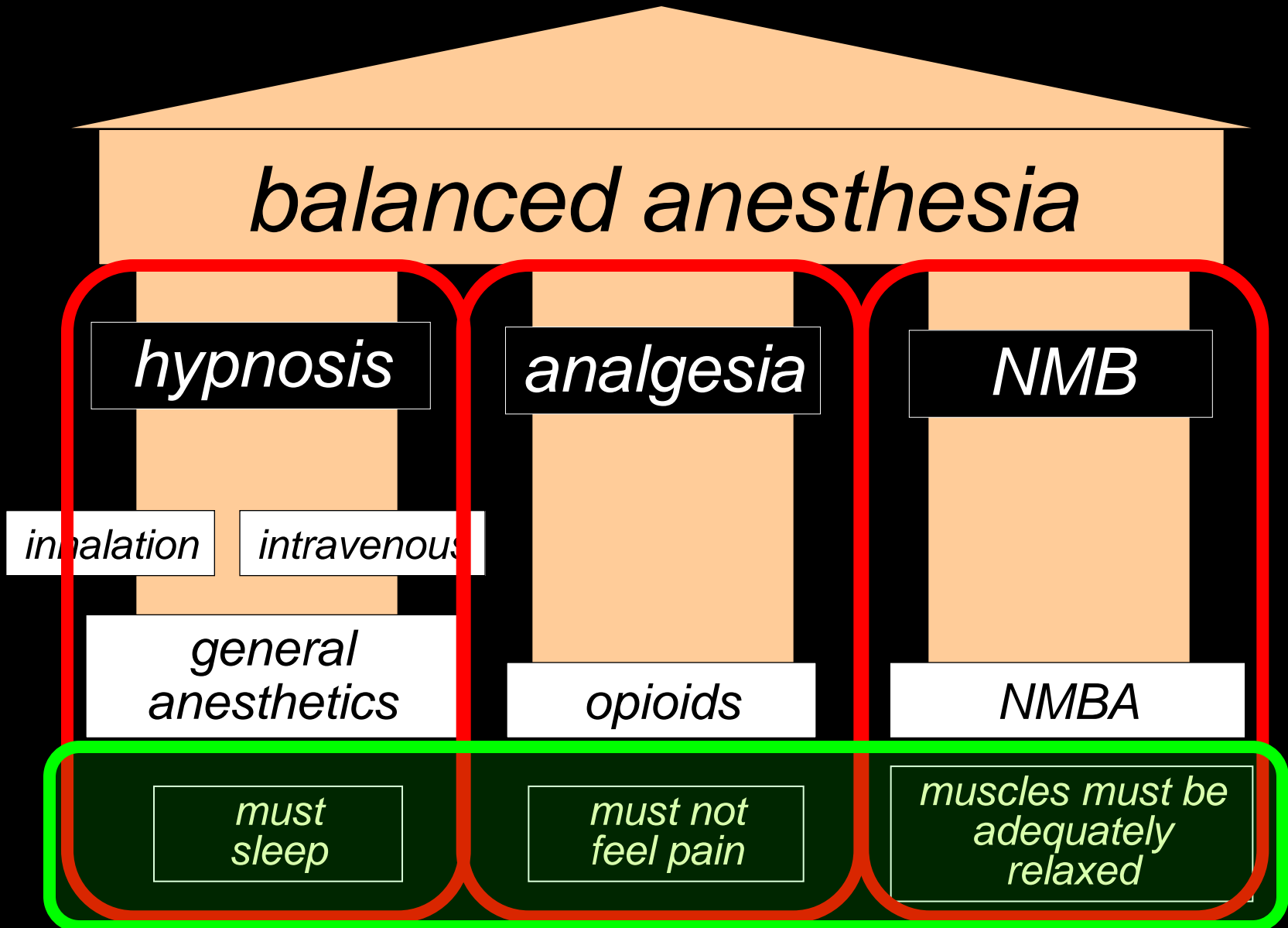
*The last birthday that's any good is 23.*

*Andy Rooney  
(1919 – 2011)*

*My diseases are an asthma, and a dropsy, and what  
is less curable, seventy-five.*

*Samuel Johnson  
(1709 – 1784)*

# NMBA as a part of balanced anesthesia



# *NMBA = powerful tool*

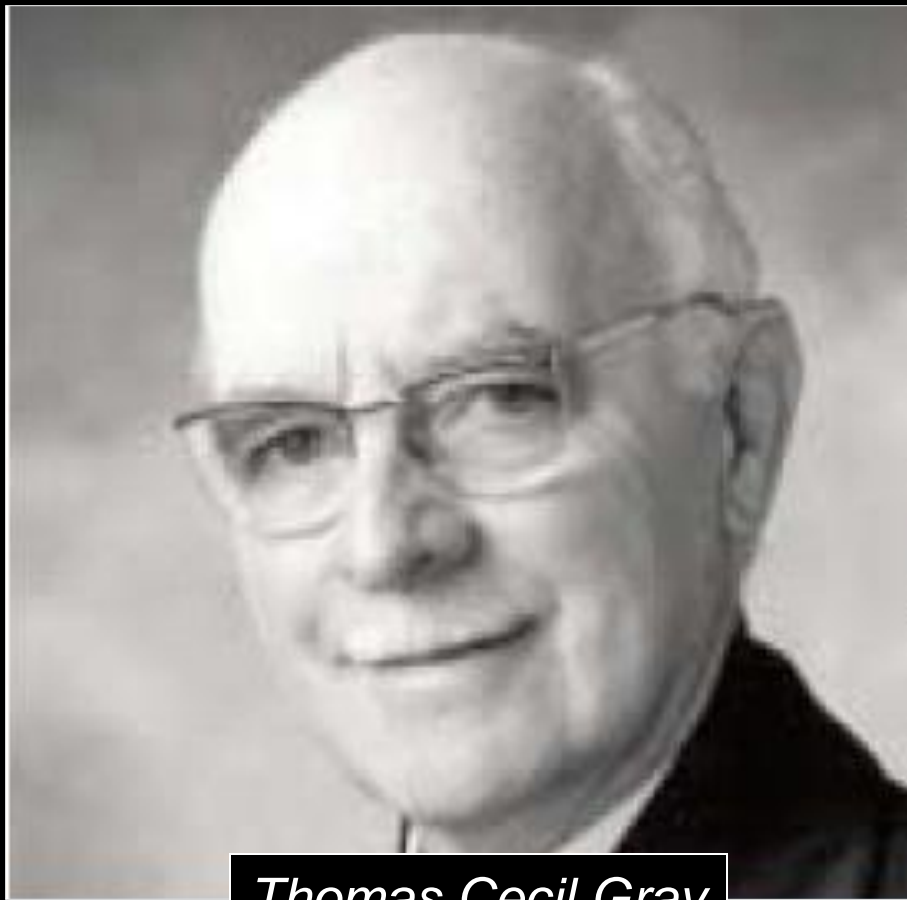
- ✓ introduction of NMBAs into clinical practice enabled the development of many surgical disciplines*
- ✗ a drug with potentially lethal effect*

# *Paradoxically ...*



*Homeopathic Hospital of Montreal, 23 January, 1942*

# „A milestone in anesthesia [d-tubocurarine chloride]”



Thomas Cecil Gray



Gray TC, Halton J:  
A milestone in anesthesia (d-tubocurarine chloride). *Proc R Soc Med.* 1946;39:400–410.

# *Anesthesia for Patients Too Sick for Anesthesia*



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[anesthesiology.theclinics.com](http://anesthesiology.theclinics.com)

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*By their very nature,  
surgical patients are “sick”  
- some more so than others.*

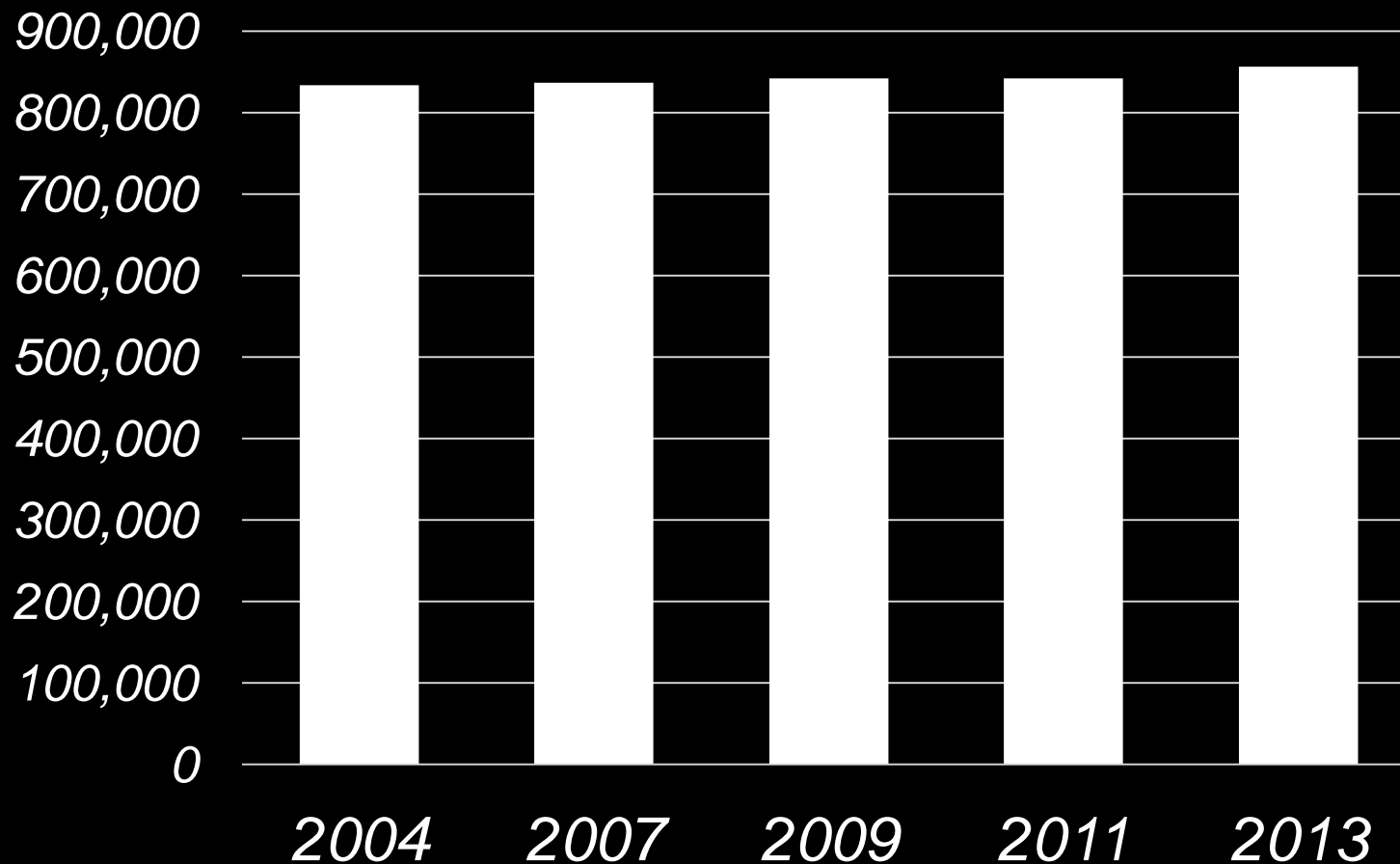
# *The population is aging*



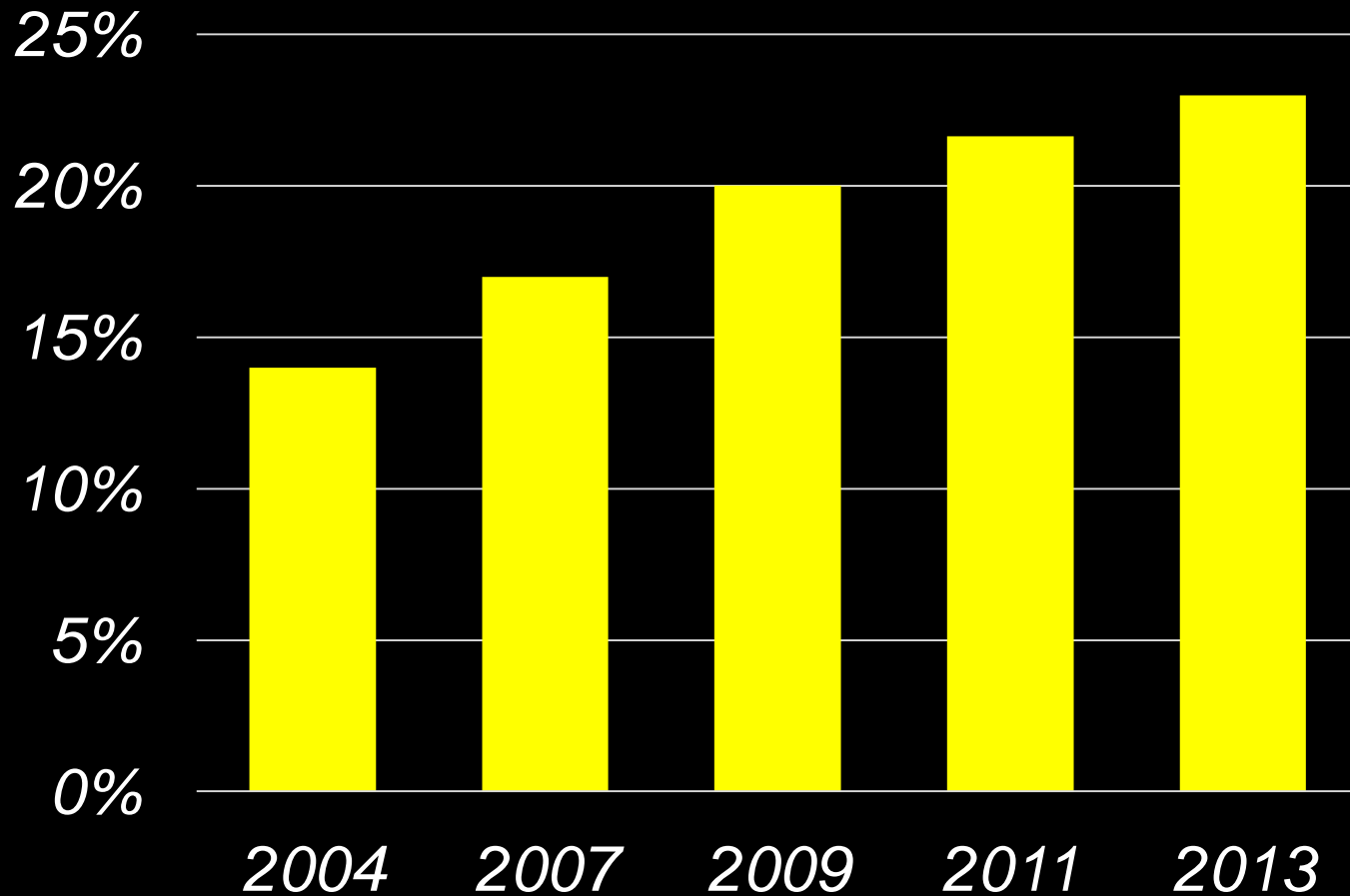
*In elderly  
there are many physiological  
and patophysiological  
changes that can influence  
both PK and PD  
of many drugs*



# *Anesthetic cases per year (CR)*



# *Proportion of seniors in the group of operated patients (CR)*





IN 2012,  
**810 MILLION**  
 PEOPLE WERE AGED 60 OR OVER.

BY 2050,  
 THE NUMBER WILL REACH  
**TWO BILLION.**

**TWO PEOPLE**

CELEBRATE THEIR SIXTIETH BIRTHDAY

**EVERY SECOND**

AN ANNUAL TOTAL OF ALMOST  
**58 MILLION** SIXTIETH BIRTHDAYS.



# *Physiological and patophysiological changes* *(different PK → PD)*

## *elderly*

- *ill (more often, more severely)*
- *co-morbidities*
- *higher ASA PS classification*
- *medication (compensation, interaction, polypragmasia)*
- *different body composition*
  - *total body water - decreased*
  - *lean body weight - decreased*
  - *total body fat - increased*

# *Physiological and patophysiological changes* *(different PK → PD)*

## *elderly*

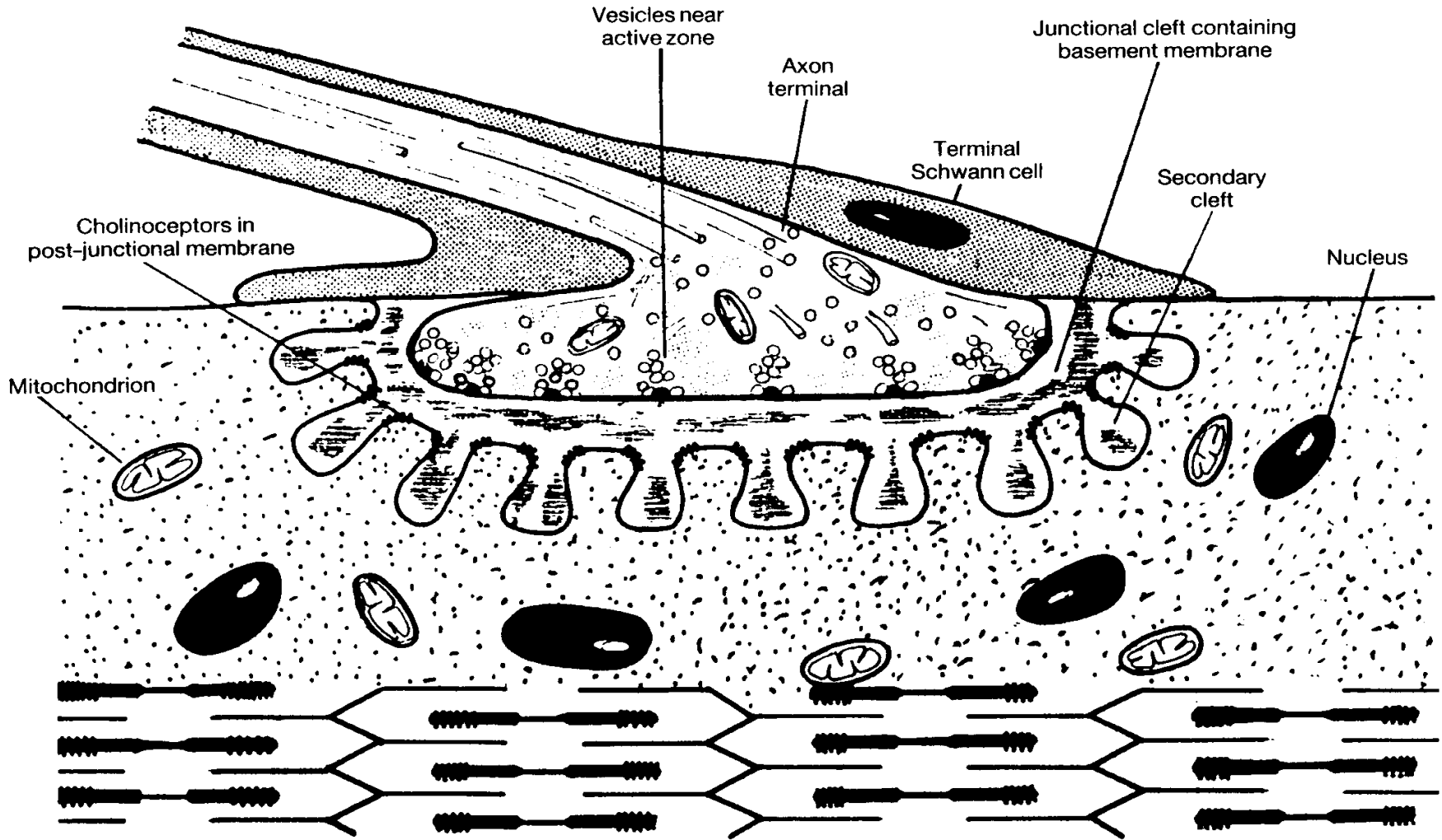
- *changes in organ functions*
  - *kidneys – decreased blood flow*
  - *liver – decreased blood flow*
  - *circulation*
    - *circulation time – increased*
    - *cardiac reserve – decreased*
- *enzyme activity – decreased*

# *Changed reactivity to drugs in elderly*

*(mechanisms)*

- 1. binding to plasma proteins*
- 2. changes in composition of body tissues*
- 3. metabolism of drugs*
- 4. pharmacodynamic parameters*

# Motor end plate



Bowman WC, Rand MJ:  
*Textbook of pharmacology. 2nd edition. Oxford: Blackwell Scient. Publications; 1980.*

# *Neuromuscular junction in elderly*

## *morphology and physiology*

- *decreased number of motor units*
- *increased number of nicotinic receptors in motor units*
- *proliferation of extrajunction receptors*
- *reduction of the amount of ACh in motoneurons*
- *decreased concentration of ACh receptors at the motor end plate*
- *increase in the distance between the axon and motor end plate*
- *flattening of the folds of the motor end plate*
- *decreased release of ACh from the preterminal axon in response to a neural impulse*
- ✗ *differences in the PD of the NMJAs do not appear to be due to changes in the neuromuscular junction*



# *Neuromuscular junction in elderly*

## *morphology and physiology*

*The ED<sub>95</sub> (dose of NMBA causing 95% neuromuscular block), is similar the elderly and young patients.*

<i>NMBA</i>	<i>ED<sub>95</sub> (mg/kg)</i>		<i>Reference</i>
	<i>young</i>	<i>elderly</i>	
<i>PANC</i>	<i>0,078</i>	<i>0,081</i>	<i>Duvaldestin et al. (1982)</i>
<i>VEC</i>	<i>0,041</i>	<i>0,038</i>	<i>O'Hara et al. (1985)</i>
<i>ROC</i>	<i>0,521</i>	<i>0,369</i>	<i>Bevan et al. (1993)</i>

# *Neuromuscular junction in elderly*

## *morphology and physiology*

*Lien CA. Nondepolarizing Neuromuscular Blocking Agents in the Elderly: Dosing Paradigms Revisited Perioperative Care For The Geriatric Patient. Prague, June, 14–16, 2009. CD-ROM.*

- when elderly patients have the same plasma concentration of NMBA as do young adults, they also have the same degree of neuromuscular block*
- differences in PD parameters, therefore, appear to be due to differences in pharmacokinetics of the NMBAs in the aged patient population.*

*Variability in effect of NMBA  
is high*

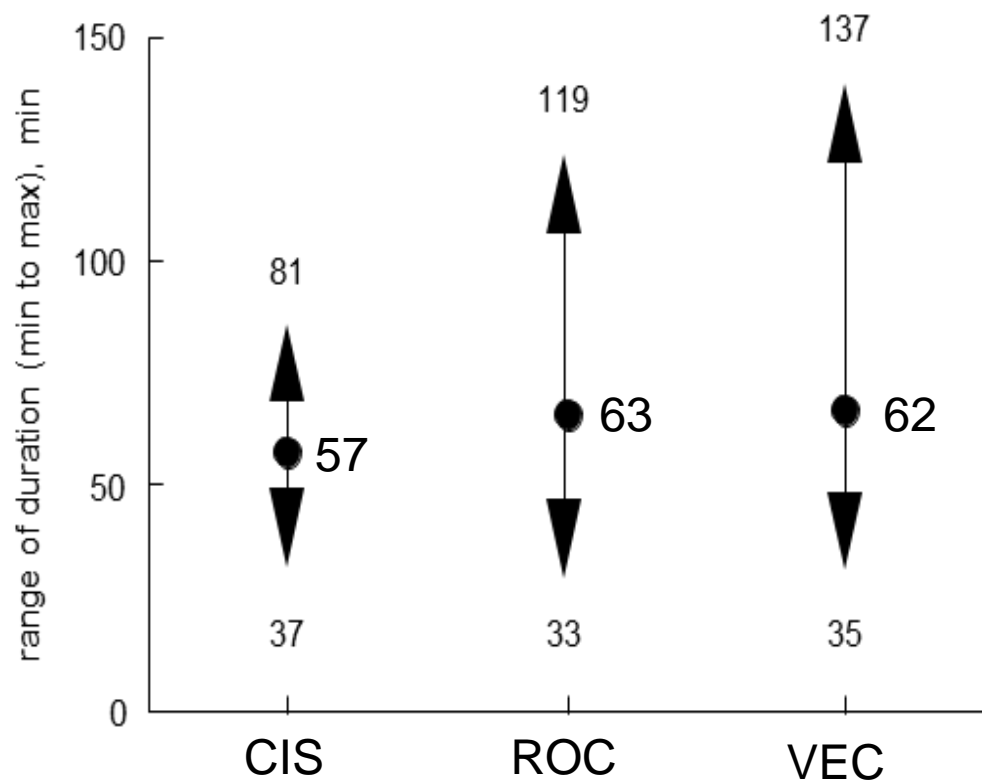
*in all patients*

*in seniors it may be further  
increased*

# Variability of duration of action of neuromuscular-blocking drugs in elderly patients

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CIS	0,1 mg/kg
ROC	0,6 mg/kg
VEC	0,1 mg/kg

*When used with sevoflurane/N<sub>2</sub>O, there was a two-fold greater variability of duration of NMB in elderly patients receiving ROC or VEC compared with CIS*

# *Elimination of NMBA*

<i>NMBA</i>	<i>elimination via</i>		
	<i>kidney</i>	<i>liver</i>	<i>others</i>
<i>PAN</i>	+++++	+	--
<i>PIP</i>	+++++	+	--
<i>VEC</i>	++	++	--
<i>ROC</i>	+	+++	--
<i>ATR</i>	+	--	+++++
<i>CIS</i>	+	--	++++
<i>MIV</i>	+/-	--	+++++

# Suxamethonium

Anesthesiology  
53:517–520, 1980

Correlation of Succinylcholine Duration of Action with Plasma Cholinesterase Activity  
in Subjects with the Genotypically Normal Enzyme

JØRGEN VIBY-MOGENSEN, M.D.\*

*elderly – decreased activity of plasma cholinesterase  
the decrease is insufficient to prolong the effect of SUX*

*possible interactions – prolonged effect of SUX:  
donepezil (Aricept)*

- *therapy of Alzheimer disease*
- *reversible inhibitor of AChE*
- *biological half-time 70 hrs*

## ***Pharmacokinetics and Pharmacodynamics of Cisatracurium in Young and Elderly Adult Patients***

Shahpoor S. Sorooshian, F.R.C.A.,\* Michael A. Stafford, M.Sc., F.R.C.A.,† Nigel B. Eastwood, B.Sc., F.R.C.A.,‡ Alastair H. Boyd, F.R.C.A.,‡ Christopher J. Hull, F.R.C.A.,§ Peter M. C. Wright, M.D., F.F.A.R.C.S.I.†

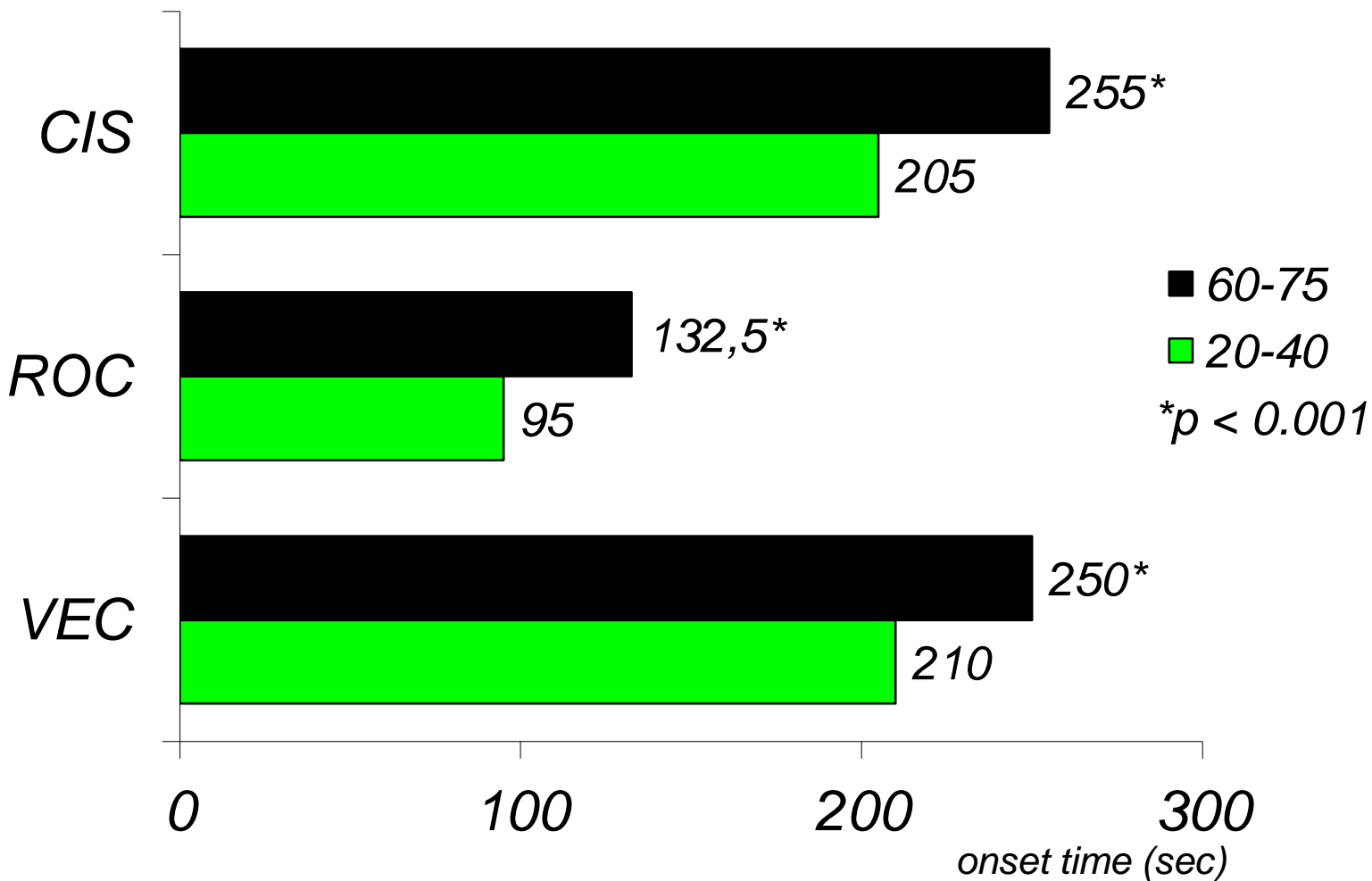
- *young (18–50 yrs) vs. elderly (over 65 yrs) patients*
- *CIS 0,1 mg/kg + 0,025 mg/kg boluses (or infusion)*
- *blood samples to determine CIS plasma concentration*
- *pharmacokinetics modeling*
- *TOF measurements*

*PK of CIS differs only marginally between young and elderly  
onset is delayed in elderly due to slower biophase equilibration*

*× limitation of this study: gender - less males (9/22) in younger group than in elderly group (19/14)*

# Onset time (sec)

*influence of age*



Adamus M. Influence of age on the pharmacodynamic parameters of cisatracurium, rocuronium and vecuronium in males during total intravenous anaesthesia - A prospective study. *Anesteziologie a intenzivní medicína* 2010; 21(2): 78–84. Article in Czech.



# *Onset time – prolongation in seniors*

*Lien CA. Nondepolarizing Neuromuscular Blocking Agents in the Elderly: Dosing Paradigms Revisited Perioperative Care For The Geriatric Patient. Prague, June, 14–16, 2009. CD-ROM.*

## *Mechanisms:*

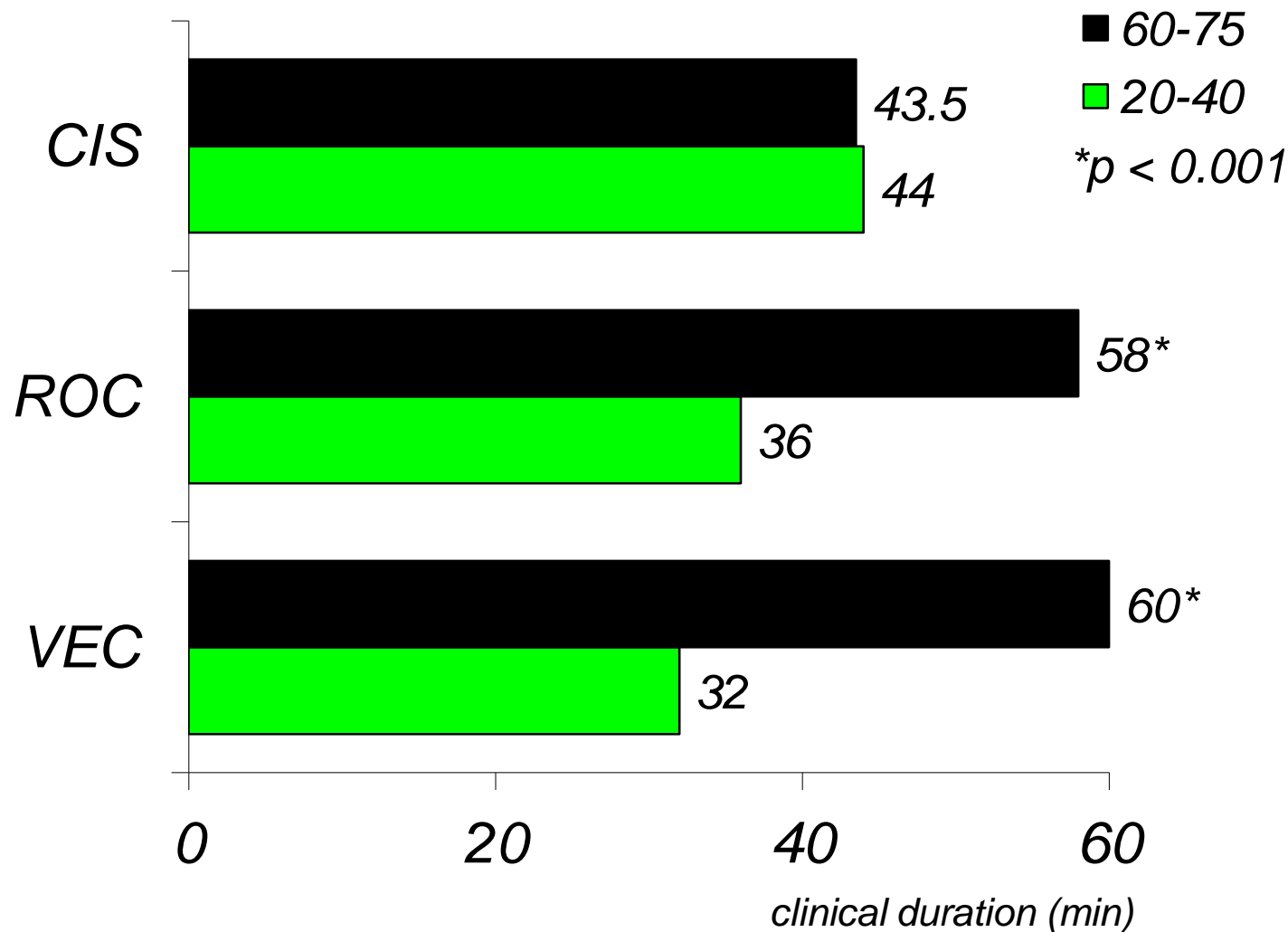
- lower cardiac output*
- longer circulation time*
- decrease blood flow to muscle*
- slower equilibration of biophases*

*onset time can be shortened: ephedrin*

*onset time can be prolonged: BB*

# Clinical duration (min)

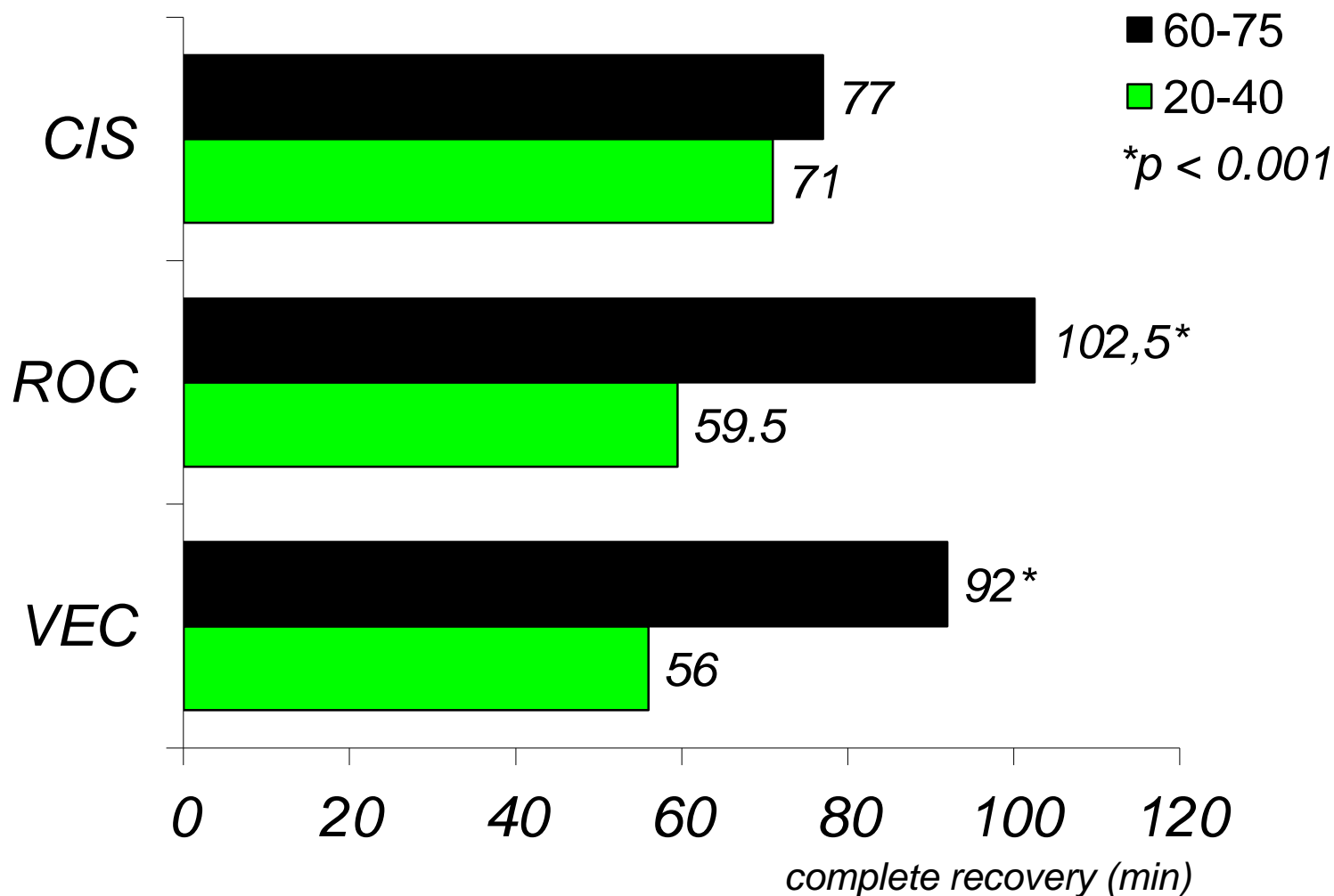
*influence of age*



Adamus M. Influence of age on the pharmacodynamic parameters of cisatracurium, rocuronium and vecuronium in males during total intravenous anaesthesia - A prospective study. *Anesteziologie a intenzivní medicína* 2010; 21(2): 78–84. Article in Czech.

# Duration to complete recovery (min)

*influence of age*



Adamus M. Influence of age on the pharmacodynamic parameters of cisatracurium, rocuronium and vecuronium in males during total intravenous anaesthesia - A prospective study. *Anesteziologie a intenzivní medicína* 2010; 21(2): 78–84. Article in Czech.

# *Reversal in elderly: neostigmine*

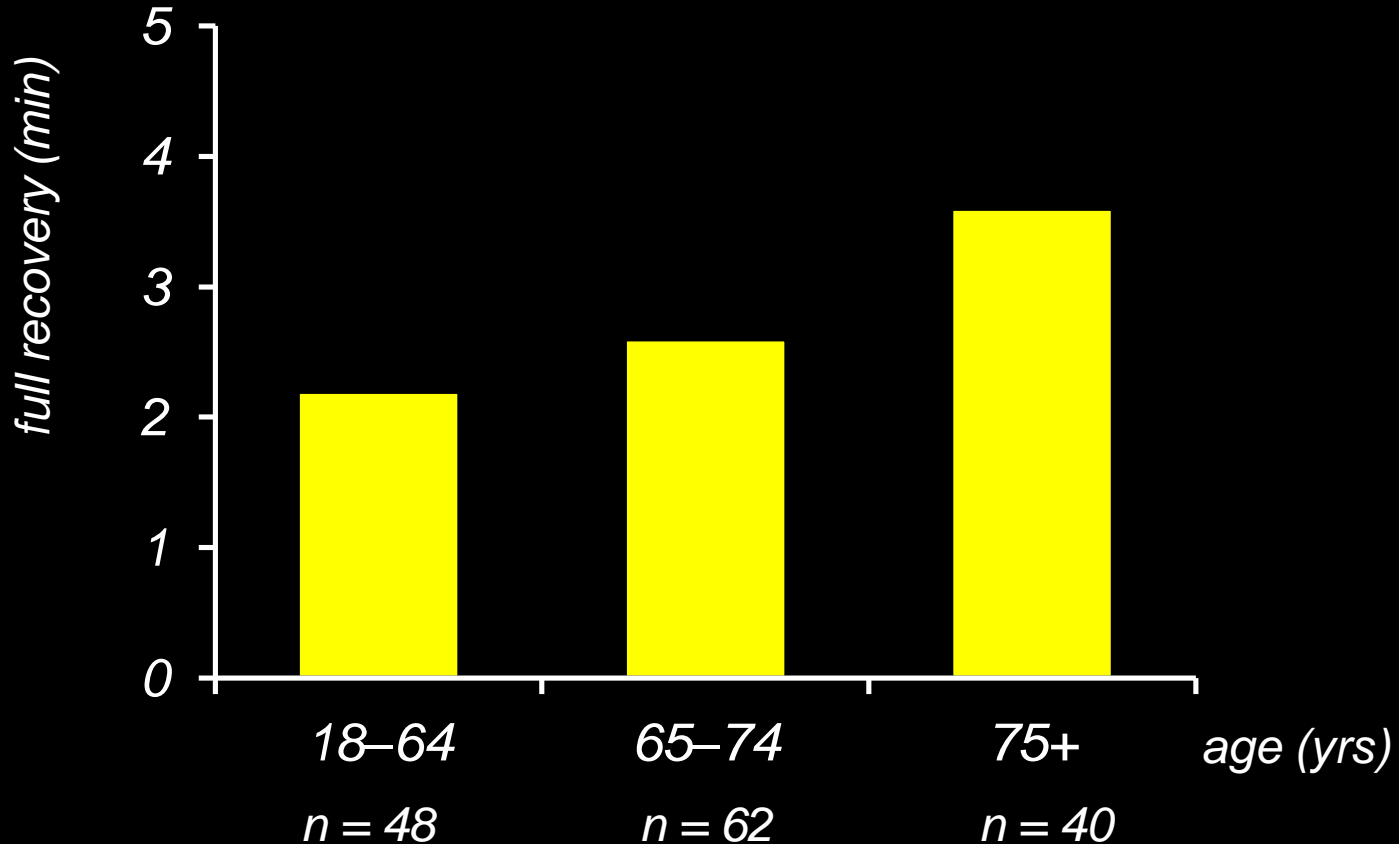
*data are not conclusive*

*most authors:*

*effect of NEO is longer than in younger*

# Reversal in elderly: sugammadex

(recommended dose is not age-dependent)



\*Reversal with *SUG* 2 mg/kg at spontaneous recovery to  $T_2$  after *ROC* 0.6 mg/kg

Data on file MSD (2008)

# *PD of NMBA's in elderly (summary)*

↑ = *prolonged*      ↔ = *unchanged*

	<i>onset time</i>	<i>clinical duration</i>	<i>full recovery</i>
<i>SUX</i>	↑	↔	↔
<i>aminosteroids</i> ( <i>ROC, VEC</i> )	↑	↑	↑
<i>benzylisoquinolines</i> ( <i>CIS, ATR</i> )	↑	↔	↔

# *NMB in elderly: safe use*

- *is the NMB actually necessary?*
- *proper dose of NMBA is enough!*
- *titration of the NMBA dose may be useful*
- *compared to younger patients:*
  - *doses of NMBA should not be larger than recommended in younger patients*
  - *intervals of administration should not be more frequent than used in younger patients*
- *which NMBA?*
  - *steroids – excellent reversal agent is available*
  - *benzylisoquinolines – effect less dependent on organ function*
- *prolonged duration of effect of the NMBA should be anticipated*
- *objective monitoring of NMB should be used*





*NMBA? YES  
but  
BE PREPARED! (not only in elderly)*

