Respiratory Depression and Considerations for Monitoring Following Ophthalmologic Surgery

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Disclosures

I have no financial relationships to disclose.

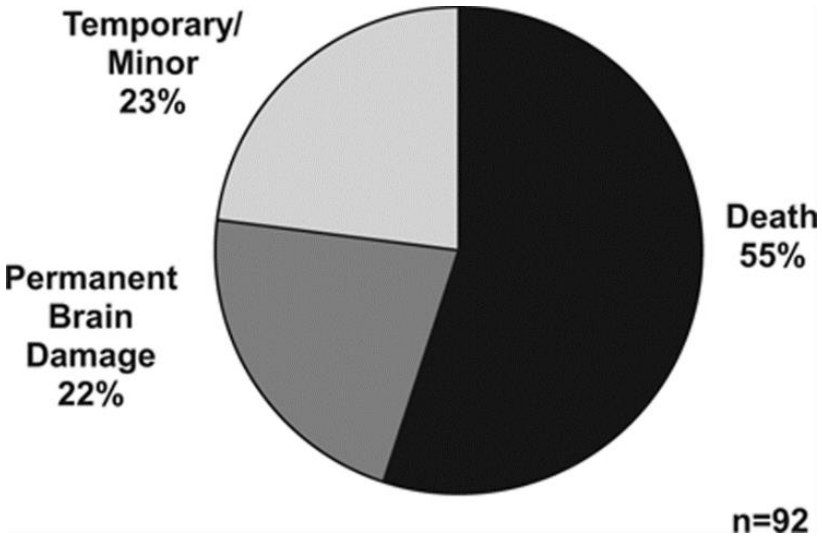
I will not discuss off label use or investigational use in my presentation.

Learning Objectives

1. To discuss the impact of sedation and General Anesthesia (GA) on postoperative respiration.

2. To review the efficacy of postoperative monitoring in capturing respiratory depression.

Postoperative Opioid-induced Respiratory Depression: A Closed Claims Analysis



Lee et al. Anesthesiology. 2015

Risk Factors

33% involved **multiple prescribers**

34% received concurrent **non-opioid sedatives**

31% received **inadequate assessment** or response

Lee et al. Anesthesiology. 2015

Additional Observations

Discovery within 2 hours: 42% **15 minutes: 16%**

Somnolence was present in 62% of patients

2/3 of patients were **obese**

1/4 of patients had either diagnosed or suspected **OSA** based on Stop Bang criteria

.

Lee et al. Anesthesiology. 2015

STOP Questionnaire to Screen for OSA

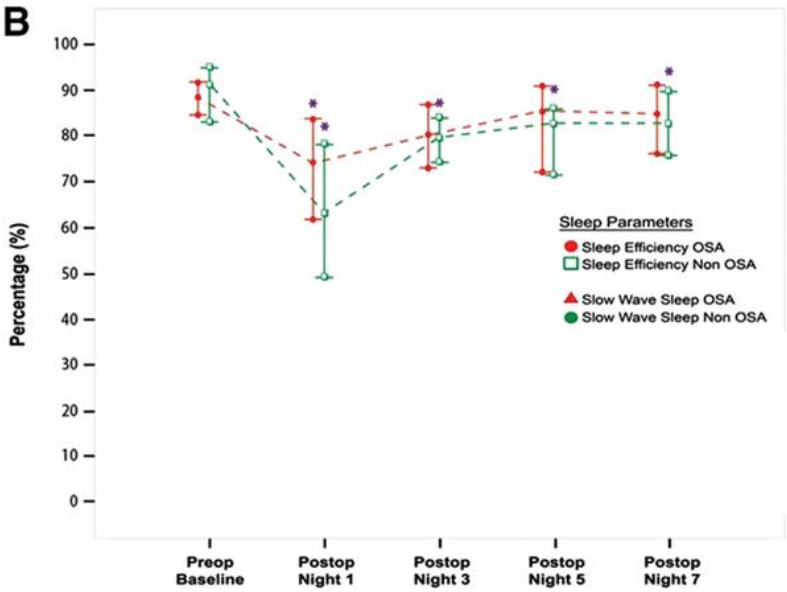
1. **Snoring** Do you snore loudly (louder than talking or loud enough to be heard through closed doors)? Yes No
2. **Tired** Do you often feel tired, fatigued, or sleepy during daytime? Yes No
3. Observed Has anyone observed you stop breathing during your sleep? Yes No
4. **Blood pressure** Do you have or are you being treated for high blood pressure? Yes No
5. **BMI** BMI more than 35 kg/m2 ? Yes No
6. **Age** Age over 50 yr old? Yes No
7. **Neck circumference** Neck circumference greater than 40 cm? Yes No
8. **Gender** Gender male? Yes No High risk of OSA: answering yes to three or more items Low risk of OSA: answering yes to less than three items

Chung et al. Anesthesiology. 2008

88% of events occurred within first 24 hours of surgery

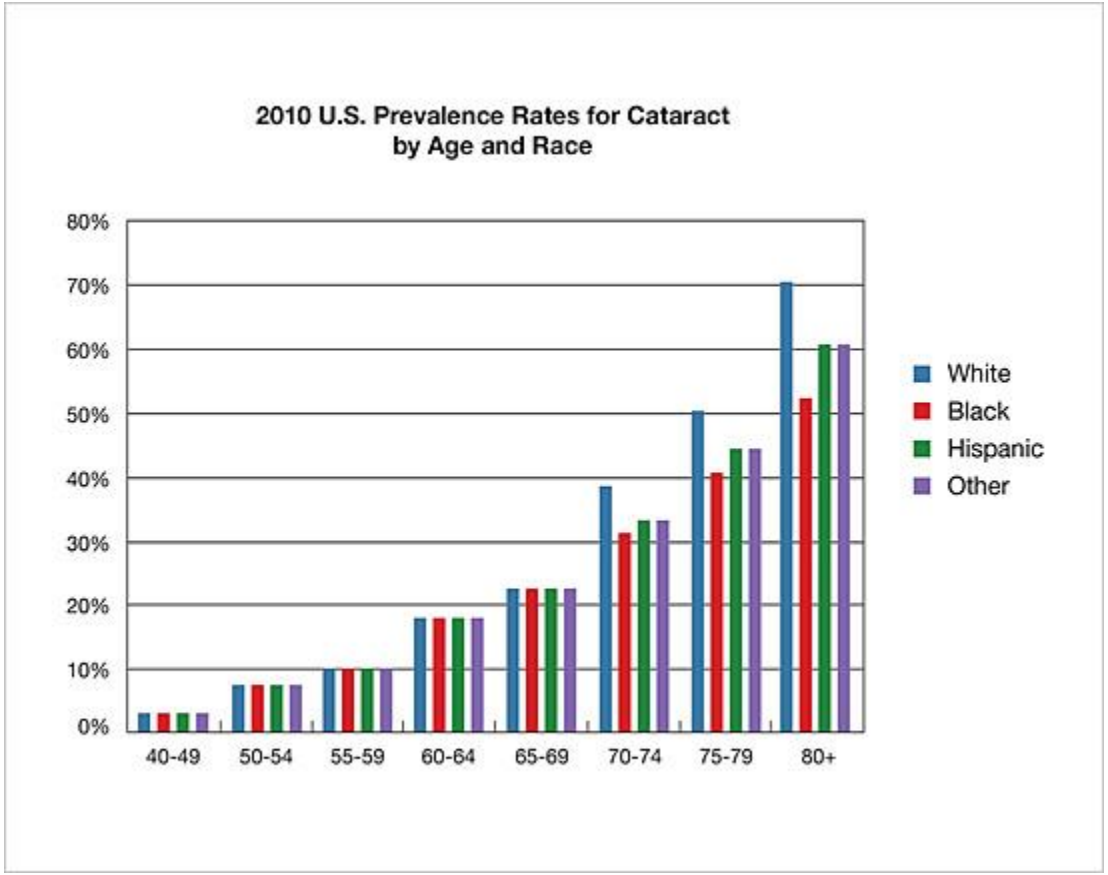
Lee et al. Anesthesiology. 2015

Why did12% of events occur after POD1?

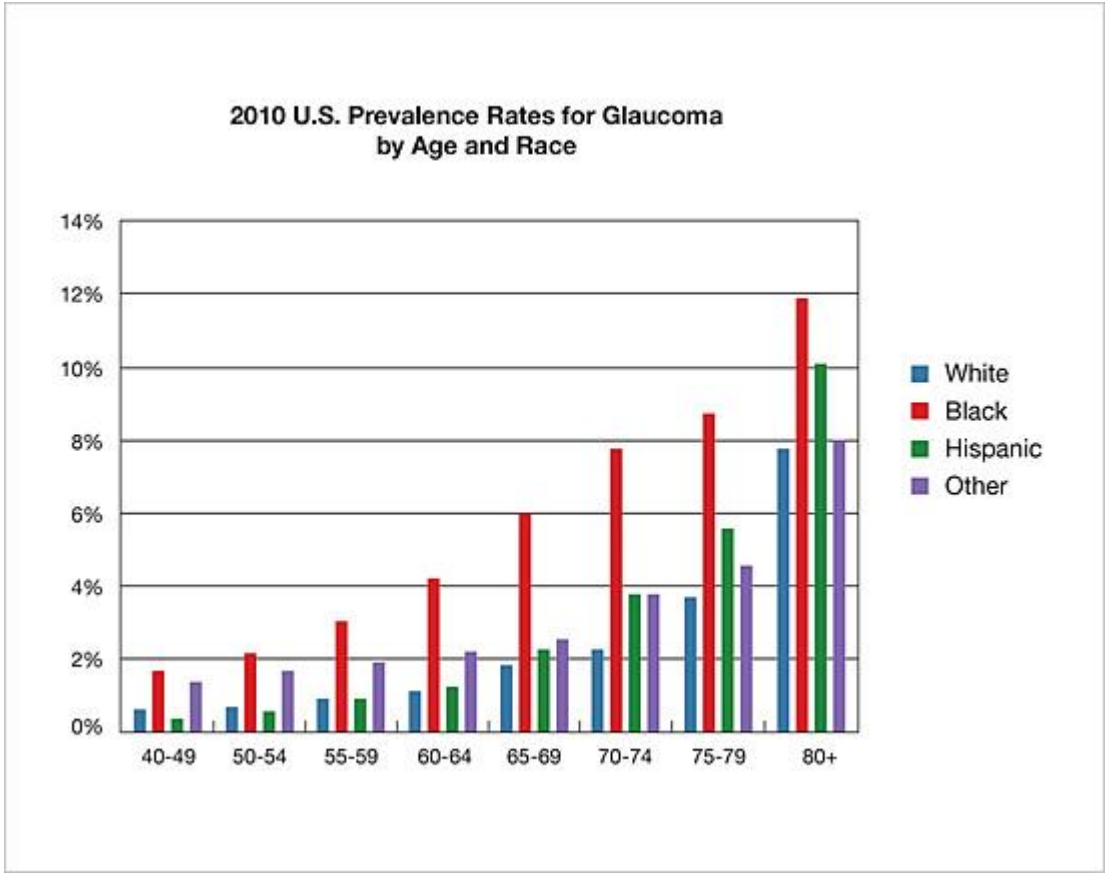


AHI, events per hour		Preop	N1	N3	N5	N7
Non-OSA	20	2 (1, 4)	3 (1, 23)*	8 (2, 18)*	3 (1, 22)	4 (1, 9)
OSA	38	18 (10, 33)†	20 (8, 43)	29 (14, 57)*†	22 (10, 38) †	21 (11, 28)†

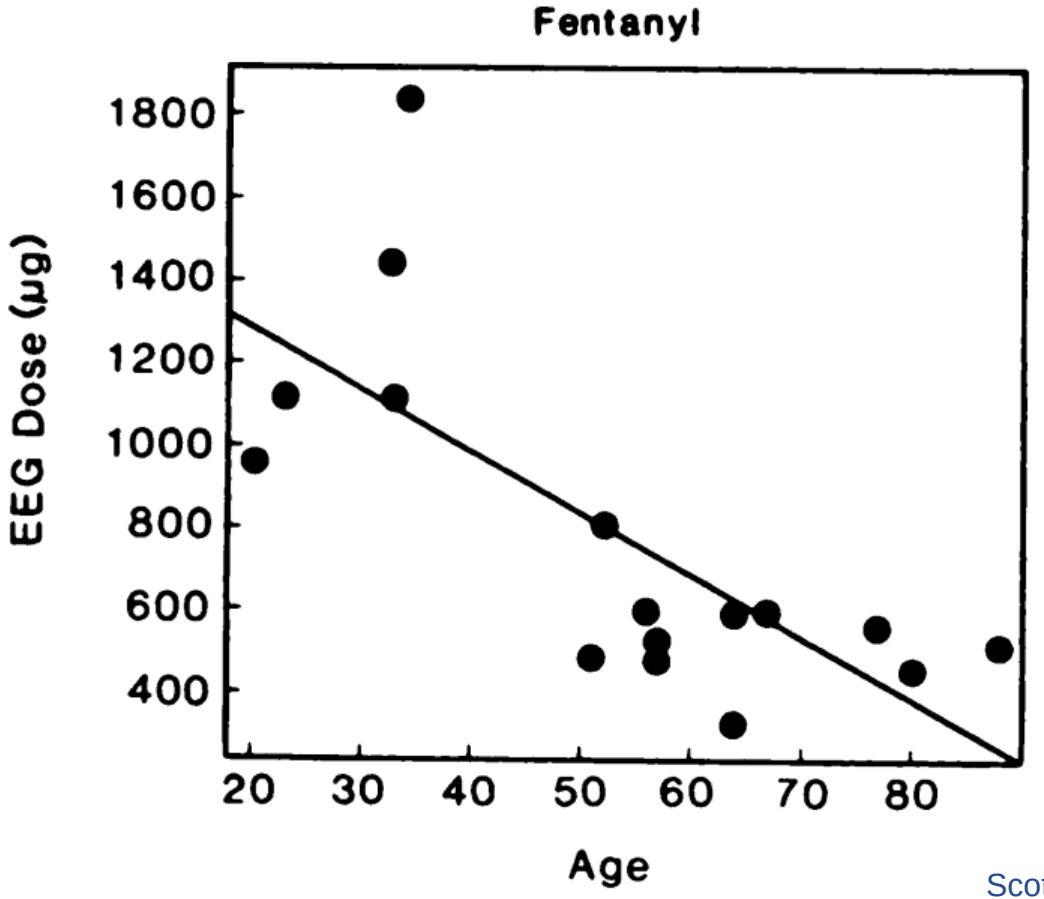
Modified. Chung et al. Anesthesiology 2014.



https://nei.nih.gov/eyedata/cataract

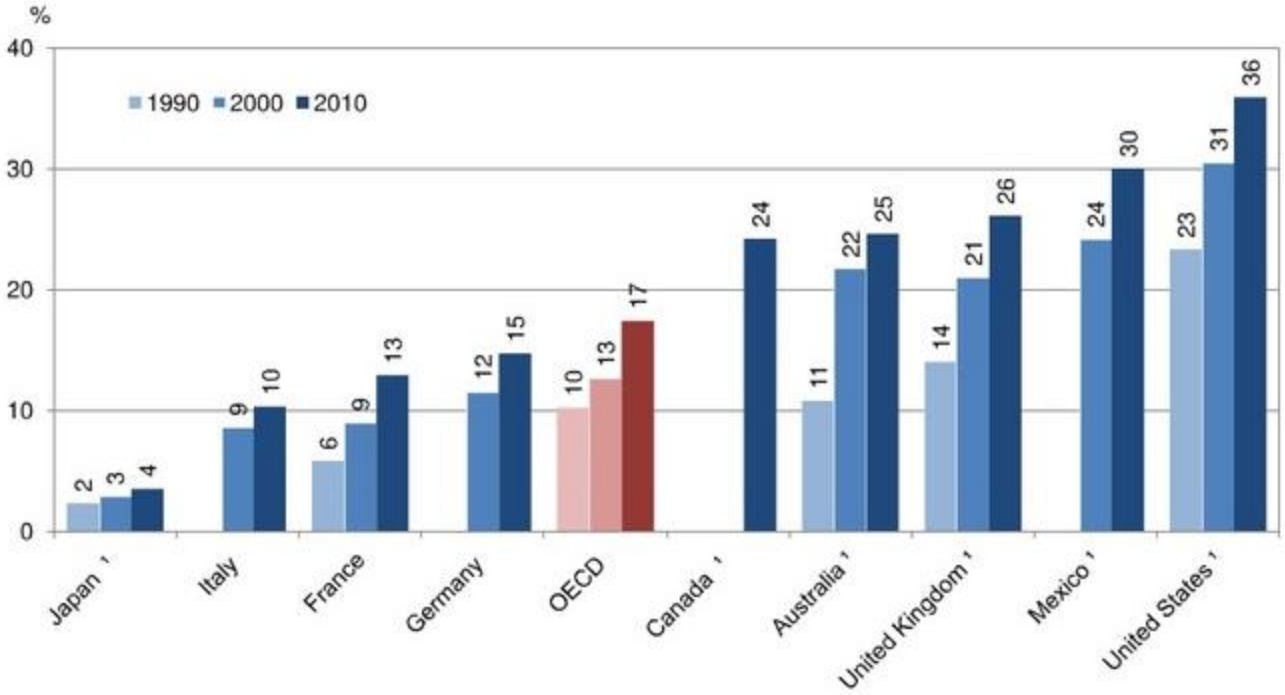


https://nei.nih.gov/eyedata/glaucoma

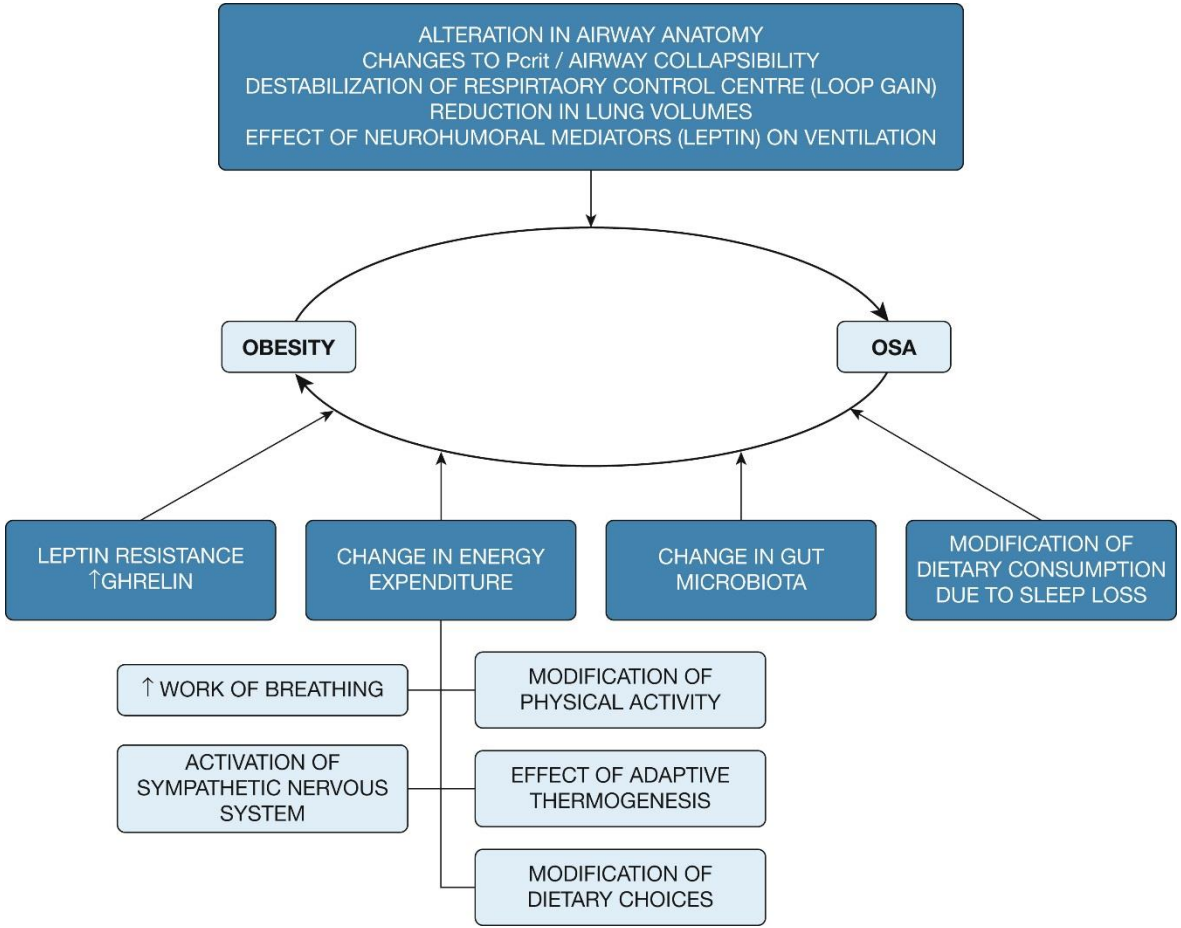


Scott et al. J Pharmacol Exp Ther. 1987

Obesity rates have increased substantially over the past 20 years and are highest in the US



1. Data are based on measurements rather than self-reported height and weight.
Source: OECD Health Data 2012.



Joosten et al. Chest. 2017

Association between OSA and Ophthalmologic Disease

Sleep Breath (2016) 20:1145–1154

Study name	Statistics for each study					Glaucoma / Total		Relative weight
	MH odds ratio	Lower limit	Upper limit	Z-Value	p-Value	OSA	Control	
Lin, 2013	1.753	1.408	2.183	5.021	0.000	114 / 1012	410 / 6072	1.43
Sergi, 2007	5.845	0.293	116.520	1.156	0.247	3 / 51	0 / 40	0.01
Boonyaleephan, 2008	2.053	0.479	8.804	0.968	0.333	6 / 44	3 / 42	0.04
Karakucuk, 2008	8.345	0.428	162.834	1.400	0.162	4 / 31	0 / 25	0.01
Kadyan, 2000	0.872	0.087	8.756	-0.116	0.907	3 / 89	1 / 26	0.02
Lin, 2011	4.873	0.283	84.058	1.090	0.276	12 / 209	0 / 38	0.01
Boyle-Walker, 2001	1.736	1.509	1.996	7.726	0.000	228 / 2725	3410 / 68235	3.29
Stein, 2008	1.214	1.177	1.252	12.357	0.000	4557 / 151633	50533 / 2030682	93.51
Muniesa, 2014	4.512	0.263	77.518	1.038	0.299	16 / 202	0 / 25	0.01
Aptel, 2014	1.133	0.885	1.451	0.990	0.322	240 / 6754	89 / 2826	1.66
Moghimi, 2013	5.505	0.258	117.486	1.092	0.275	2 / 51	0 / 54	0.01
Nowak, 2009	2.846	0.130	62.522	0.664	0.507	2 / 34	0 / 18	0.01
	1.240	1.204	1.277	14.273	0.000			

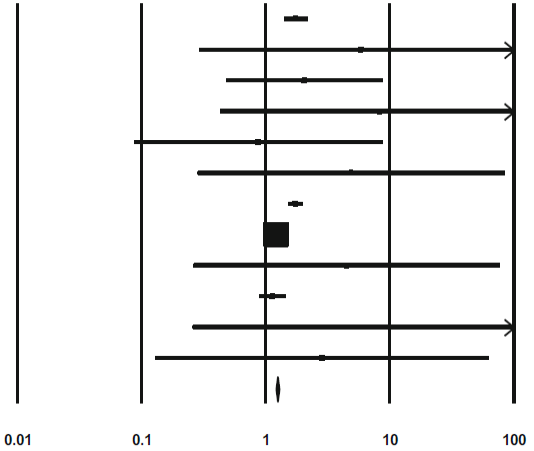


Fig. 2 Forest plots of meta-analysis of the included studies showing the odds ratios of glaucoma for subjects with and without OSA

Huon et al. Sleep Breath. 2016

Pretest

Opioids induce respiratory depression.

Pretest

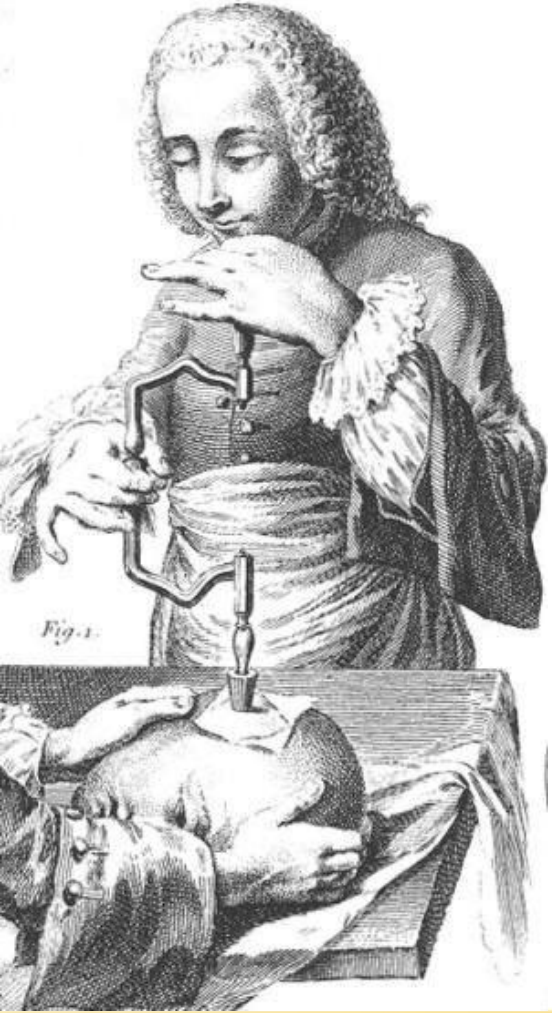
Pulse oximetry reliably captures episodes of respiratory depression in patients recovering from ophthalmologic surgery.

Pretest

Respiratory depression increases measured End Tidal CO2.

Pretest

End Tidal CO2 measurement provides reliable detection of opioid induced respiratory depression.



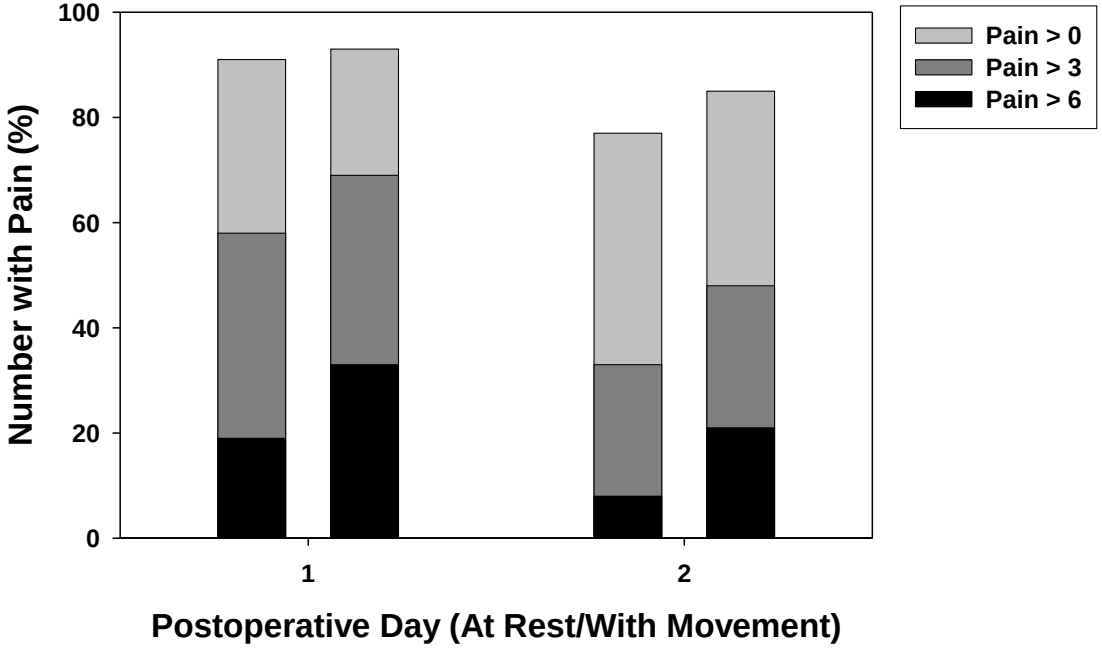
Myth

Patients do not experience intense pain following intracranial surgery.

Surgical manipulation of the brain parenchyma *per se* is not painful.

Dunbar et al., Anesth Analg. 1999

FACT: 2/3 patients report moderate to severe pain



Gottschalk et al., J. Neurosurgery. 2007

How was the pain treated?

	Percentage of Patients Treated With Opioids	P value
1st Postoperative Day	50.4	0.002
2nd Postoperative Day	32.6	0.015

Gottschalk et al., J. Neurosurgery. 2007

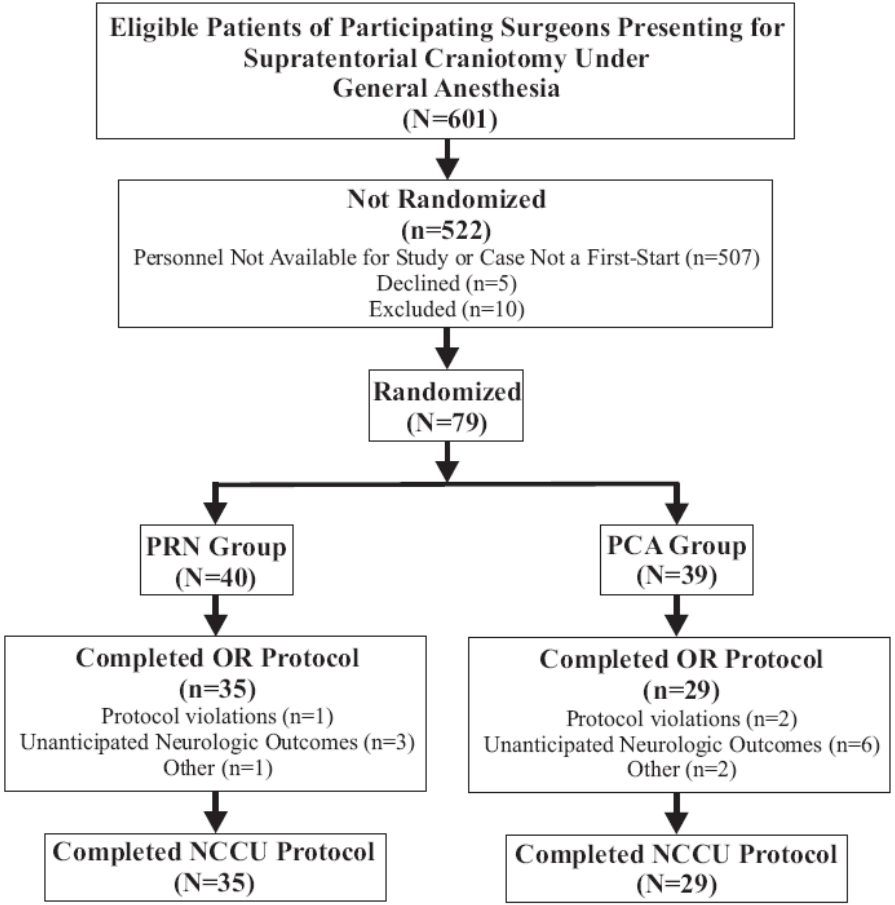
How was the pain treated?

	Percentage of Patients Treated With Opioids	P value
1st Postoperative Day	50.4	0.002
2nd Postoperative Day	32.6	0.015

Potentially **toxic doses of acetaminophen** were ordered:

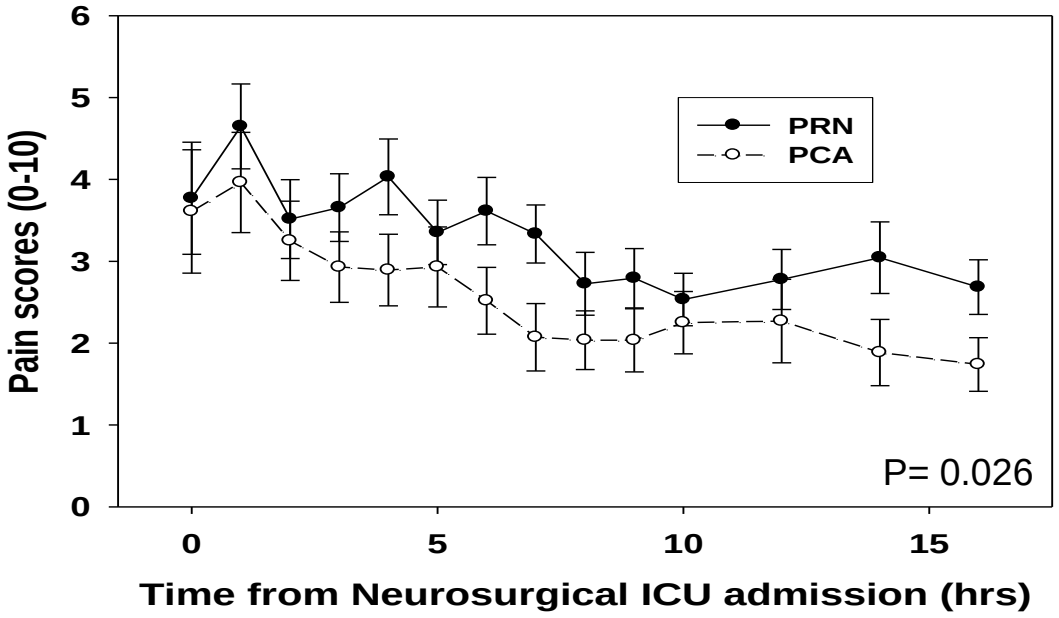
POD1: **42%** POD2: **33%**

Gottschalk et al., J. Neurosurgery. 2007



Morad et al., J Neurosurg. 2009

Supratentorial Craniotomy Pain



Morad A, et al. J Neurosurg 2009.

But is it SAFE?

Editorial

Patient-controlled analgesia

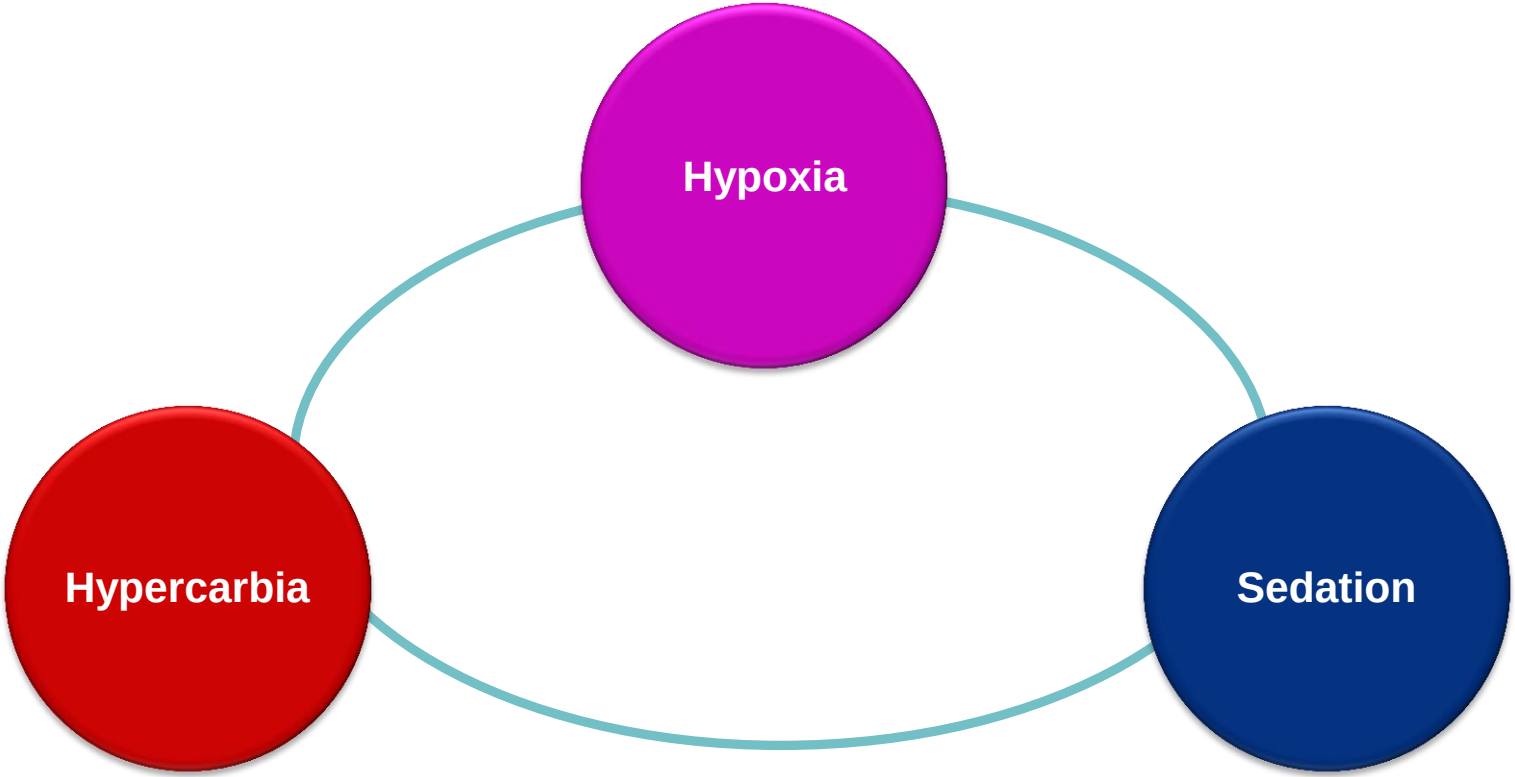
KEVIN E. VORENKAMP, M.D.[1]
MARCEL E. DURIEUX, M.D., PH.D.[1,2]

Departments of [1]Anesthesiology and [2]Neurosurgery, University of Virginia Health System, Charlottesville, Virginia

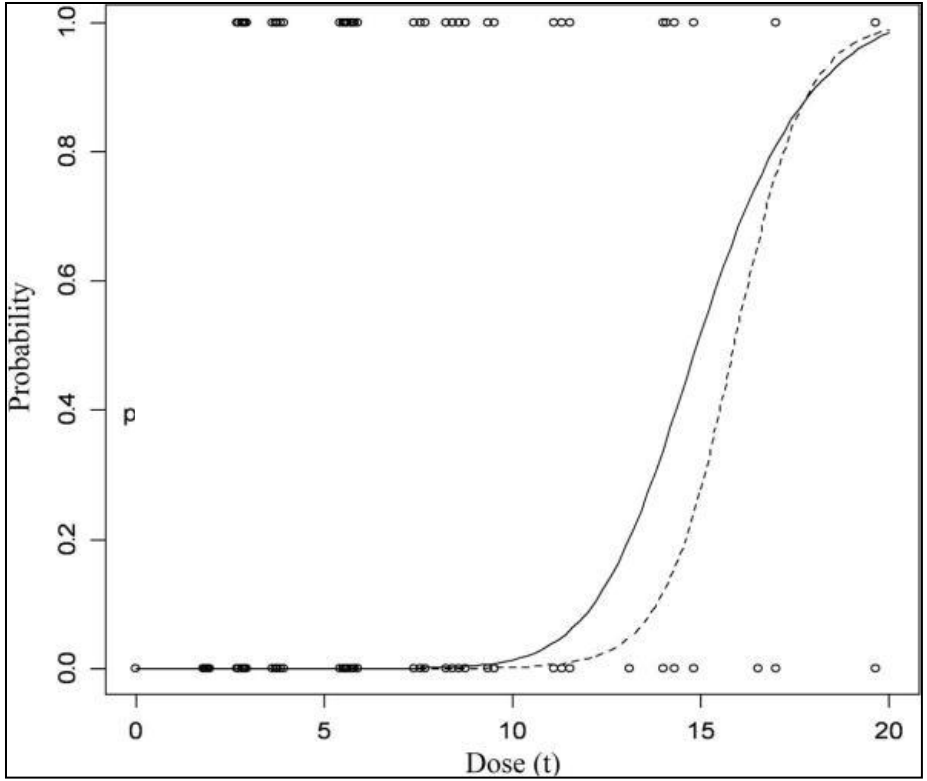
In this issue of the *Journal of Neurosurgery*, Morad

Vorenkamp et al., J Neurosurg. 2009

Major Safety Concerns Regarding Opioids

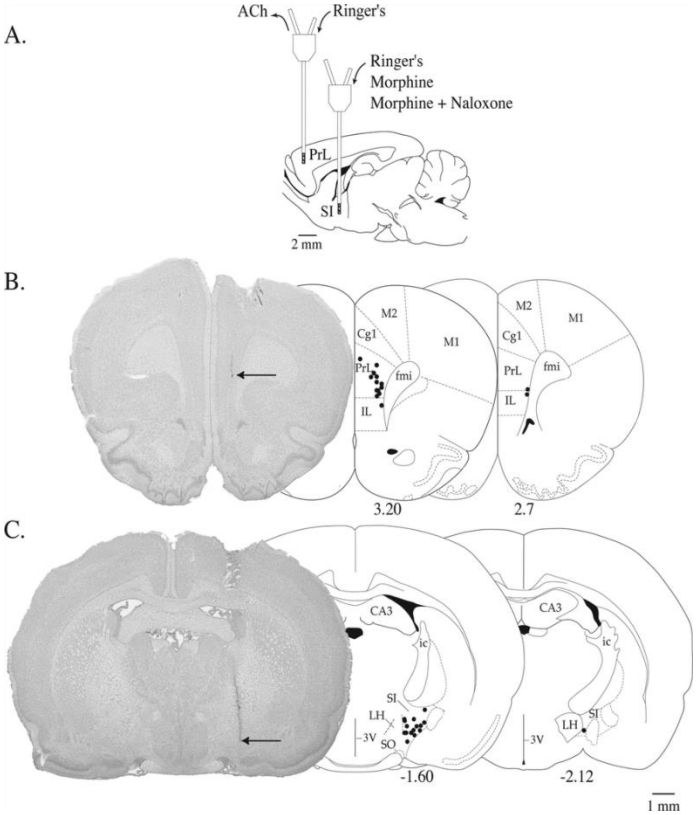


Influence of Opioids on Sedation



Hammoud et al., Pain. 2009 *modified*

A Mechanism for Opioid Induced Sedation



μ receptor activation hyperpolarizes *cholinergic neurons* projecting from the basal forebrain to the prefrontal cortex.

Osman et al., Anesthesiology. 2005

Titration of Opioids to Sedation ≠ Sufficient Analgesia

Table 3. Self-Assessment Questionnaire Regarding Postoperative Pain and Discomfort Experienced in the PACU in the Early Postoperative Period, and 24 h Postoperatively in the Ward.[a] The overall satisfaction of pain care was also recorded.

	Control group (n = 52)	Sedated group in pain (n = 26)	*P*
How are you this morning? (good/badly)	96/4	54/46	<0.0001
How did you sleep last night? (well/moderately/badly)	48/42/10	23/23/54	0.001
How is your pain this morning? (severe/moderate/no pain)	6/44/50	50/42/8	<0.0001
Yesterday, how was your pain when you arrived in your room? (severe/moderate/no pain)	18/25/57	58/16/26	0.0006
Are you satisfied with the pain care provided for the first 24 postoperative hours? (yes/moderately satisfied/no)	96/2/2	50/30/20	<0.0001

Lentschener et al., Anesth Analg. 2007

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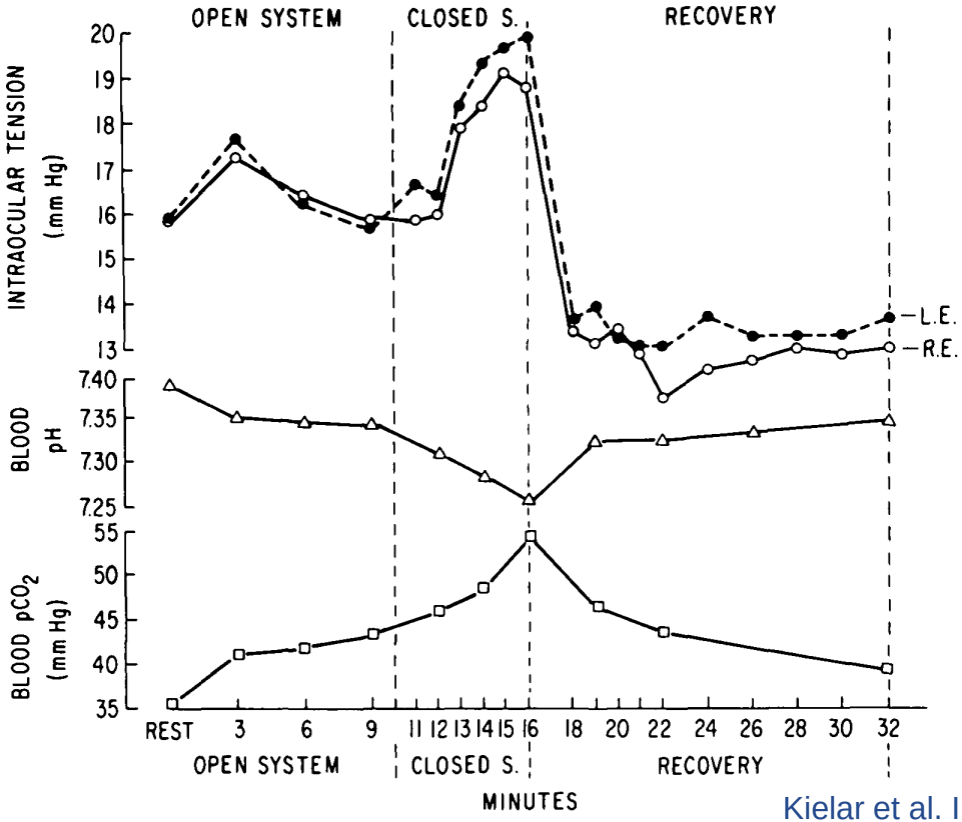
NEWSLETTER

The Official Journal of the Anesthesia Patient Safety Foundation

Volume 26, No. 2, 21-40 | Circulation 94,429 | Fall 2011

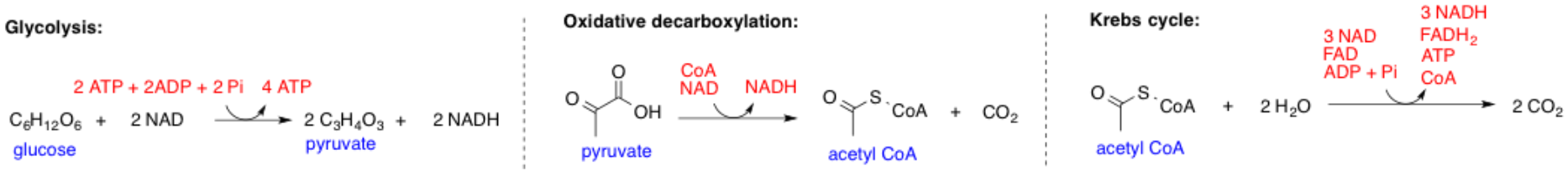
"No Patient Shall Be Harmed By Opioid-Induced Respiratory Depression"

Relation between CO2 and Intraocular Pressure



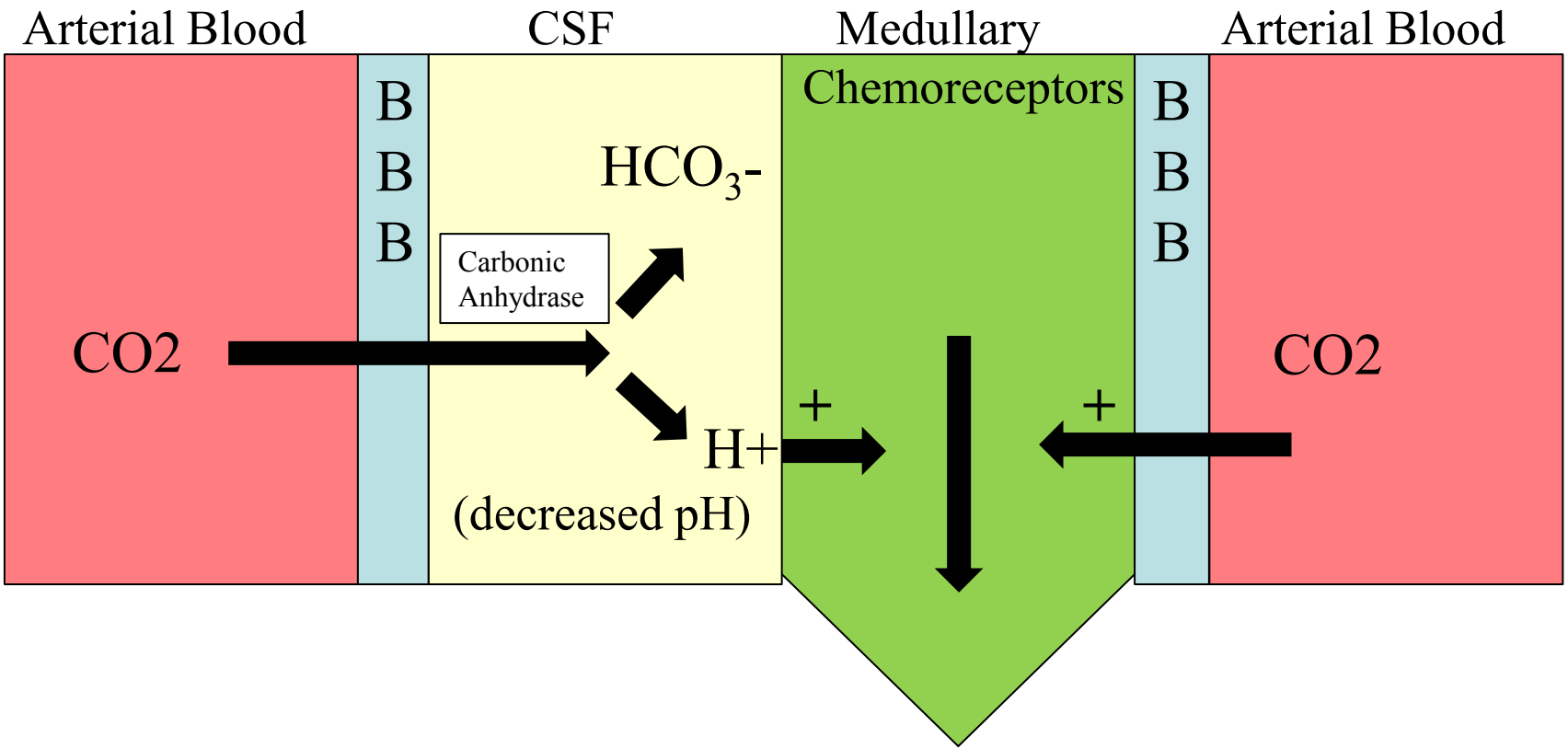
Kielar et al. Invest Ophthalmol Vis Sci. 1977

Carbon Dioxide Production



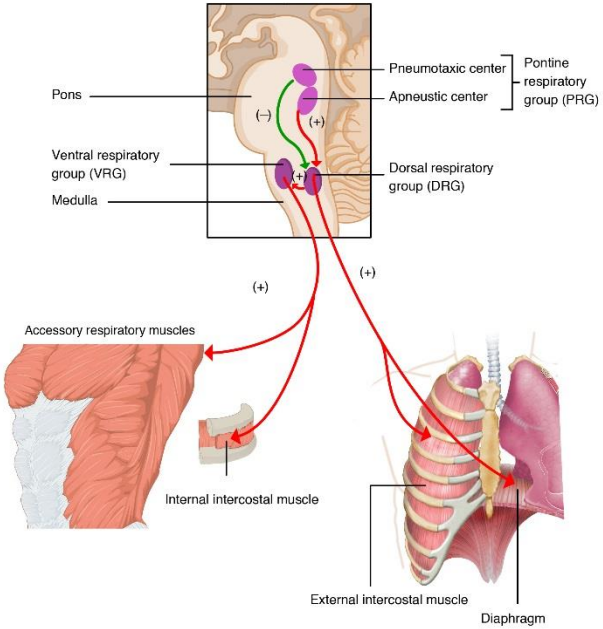
Net reactions for glycolysis of glucose, oxidative decarboxylation of pyruvate, and Krebs cycle. 2015

Carbon Dioxide Signaling- Central Chemoreceptors



Central Regulation of Breathing

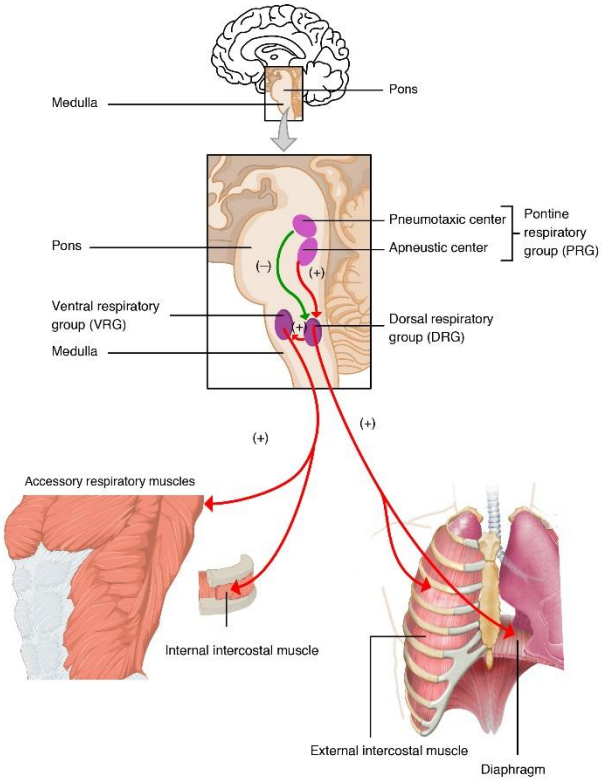
pre-Bötzinger complex (rhythm)



Respiratory centers of the brain. 2013

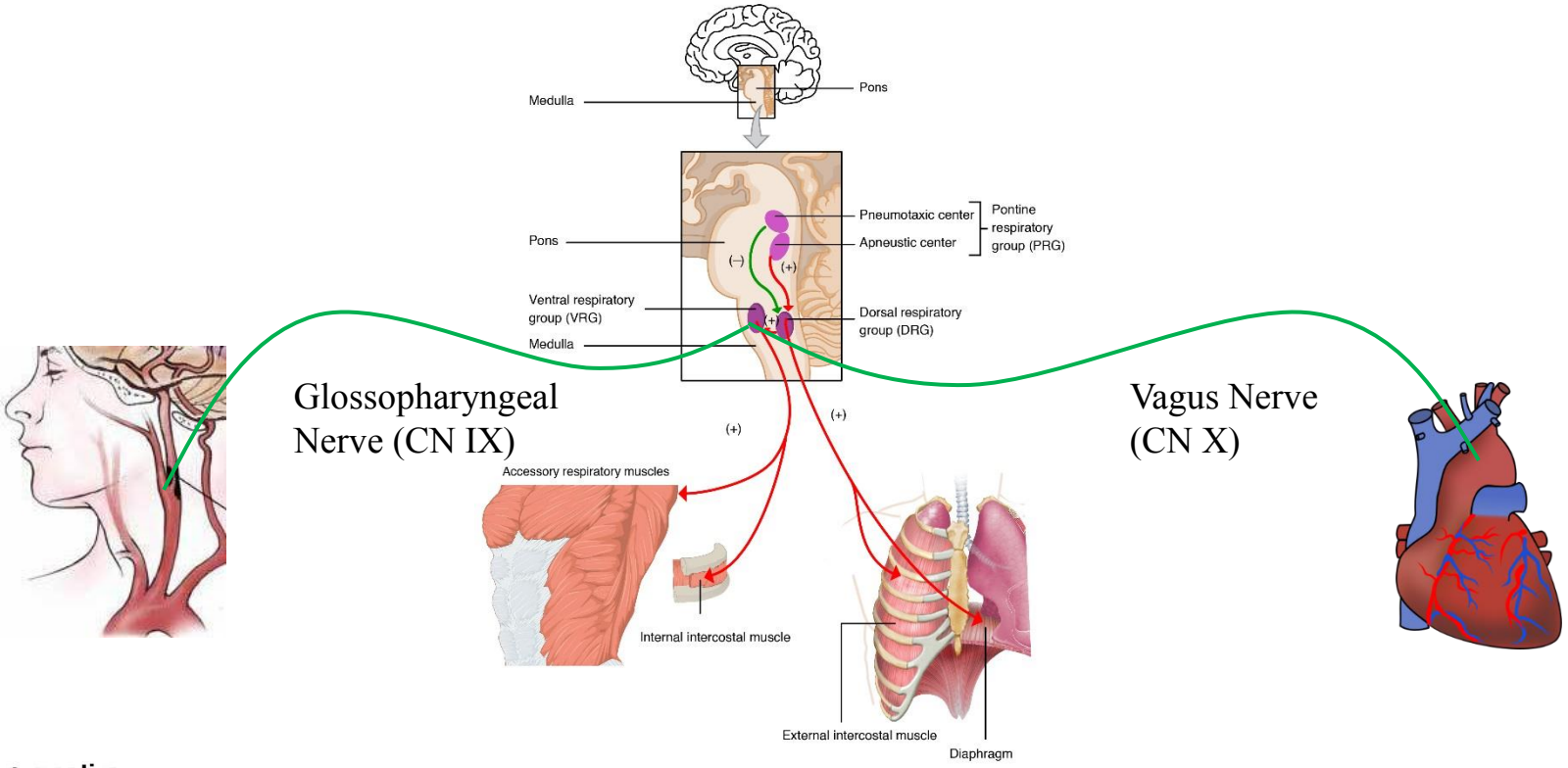
Central Regulation of Breathing

pre-Bötzinger complex (rhythm)



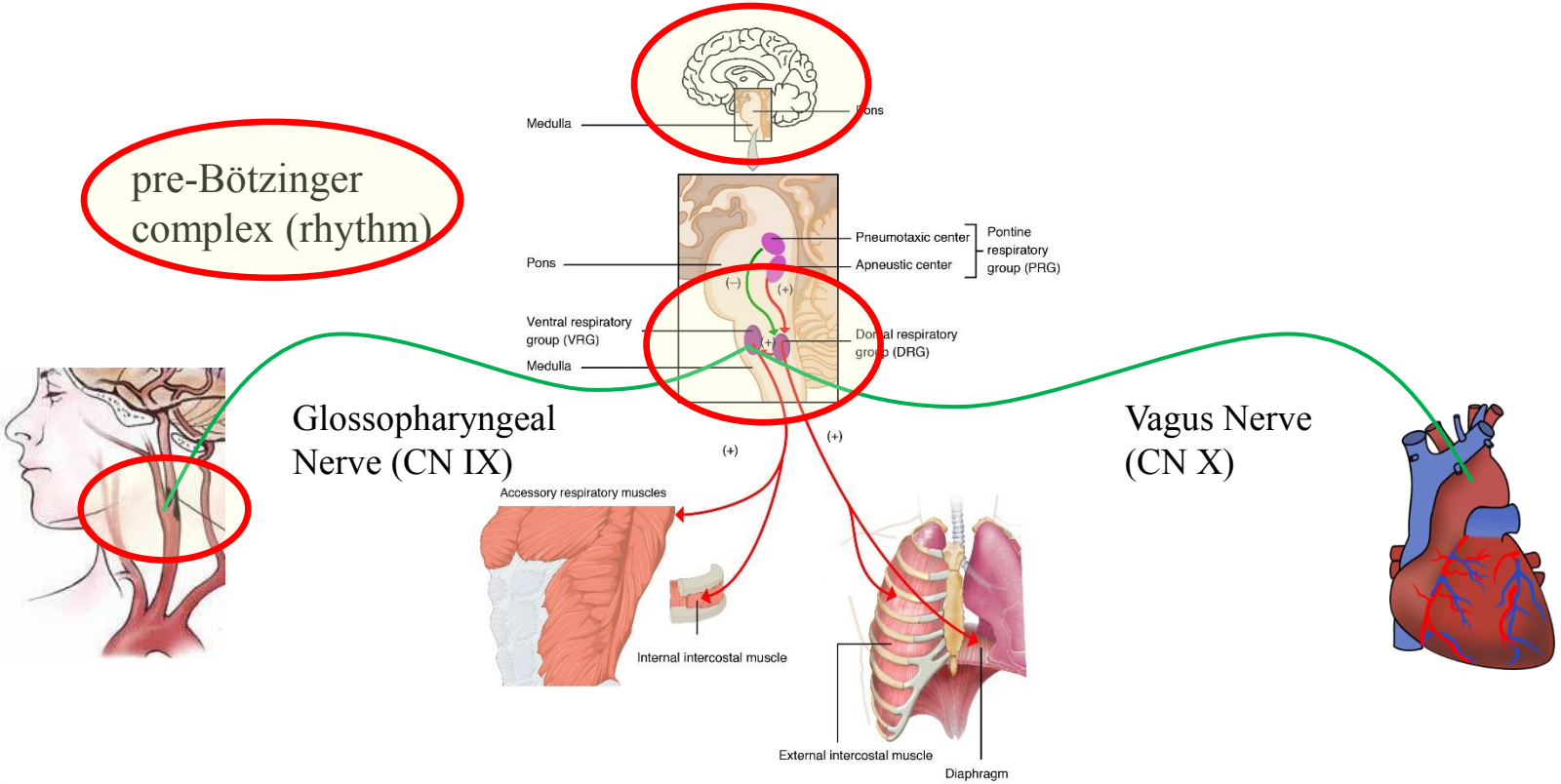
Respiratory centers of the brain. 2013

Peripheral Regulation of Breathing



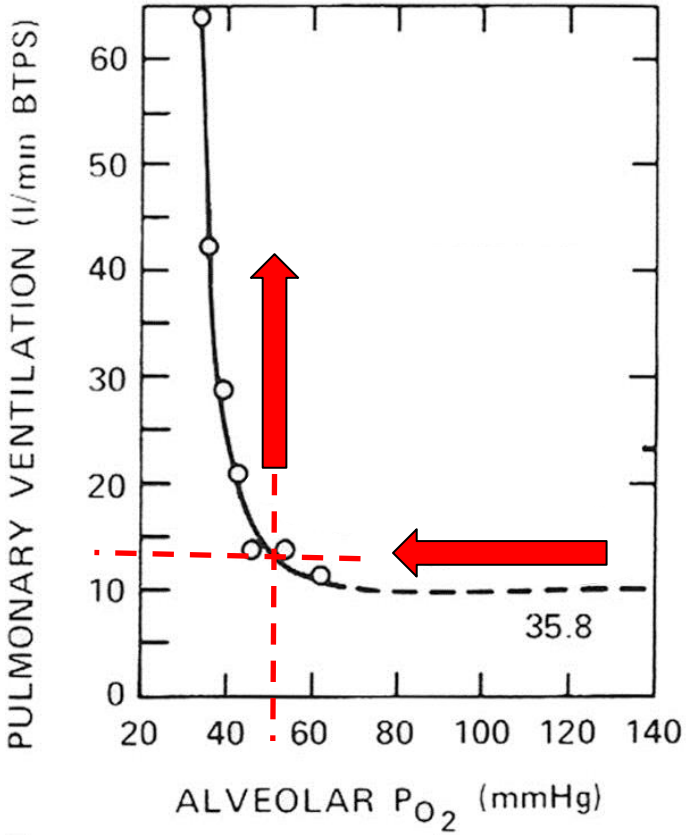
Respiratory centers of the brain. 2013

Effect of Opioids on Breathing



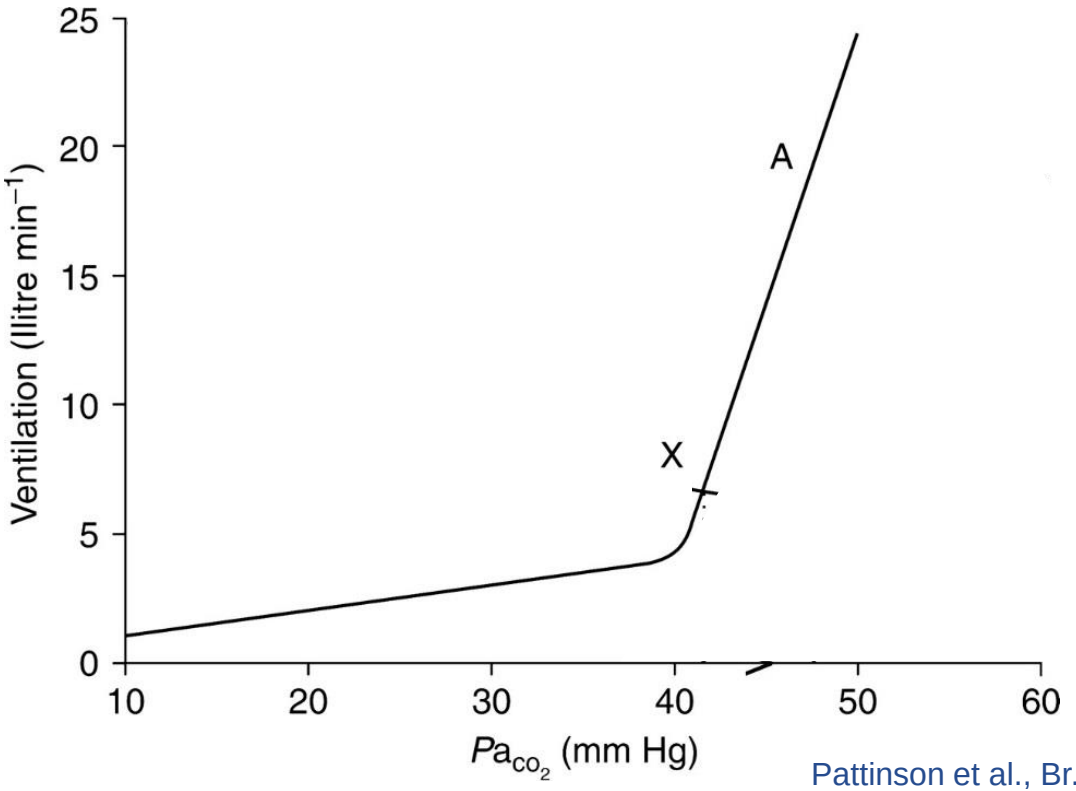
Respiratory centers of the brain. 2013

Influence of Oxygen on Respiratory Drive



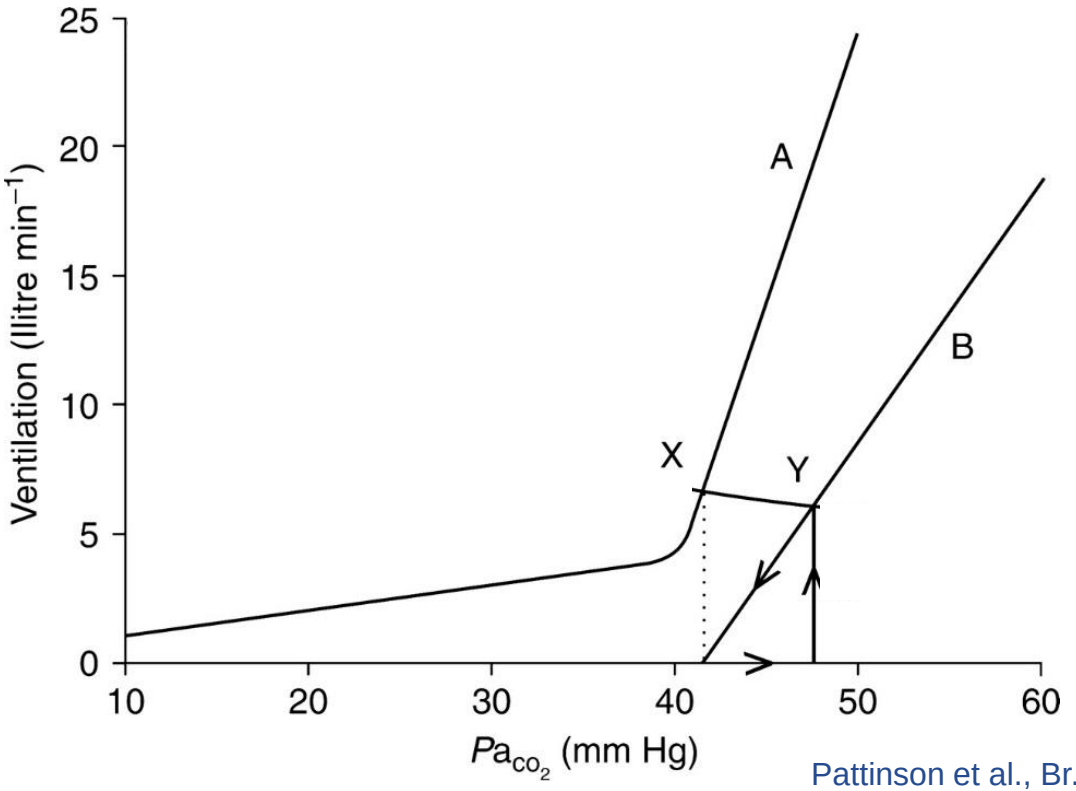
Loeschke et al., *Arch Ges Physiol*. 1958
modified

Influence of PaCo2 on Ventilation



Pattinson et al., Br. J. Anaesth. 2008 *modified*

Influence of Opioids on Ventilation



Pattinson et al., Br. J. Anaesth. 2008 *modified*

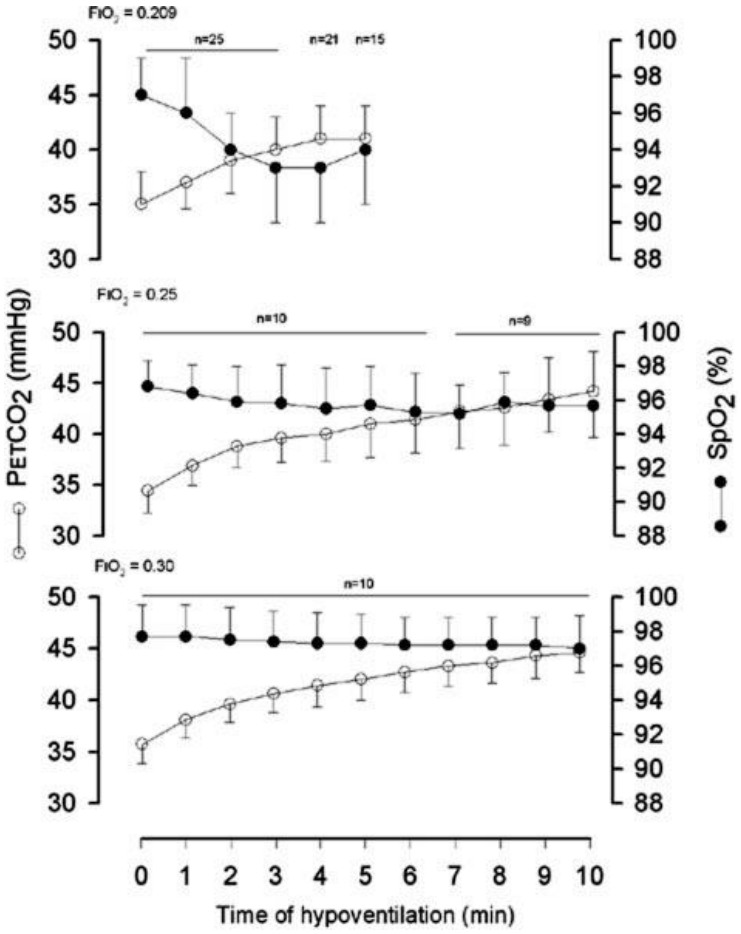
Relation between PaCO2 and PAO2

$PAO2 \approx FiO2\ (P_{ATM} - pH2O) - PaCO2/RQ$

100 mmHg ≈0.21(760mmHg-47 mmHg)-40 mmHg/0.8

PAO2 at CO2 40mmHg≈ 150-50=100

PAO2 at CO2 of 60 mm Hg≈150-75=75

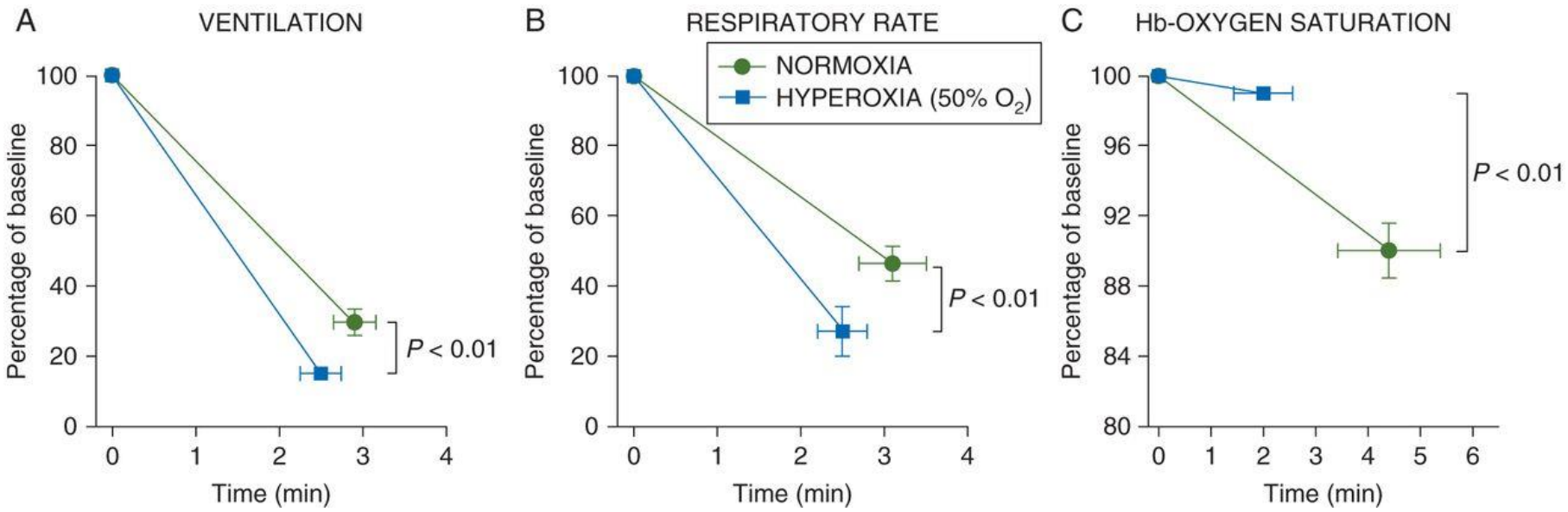


SaO2 Monitoring

Changes in SpO2 (closed) and EtCO2 (open) during hypoventilation in patients receiving FiO2 of 21%, 25%, and 30%

Fu et al., Chest. 2004

Effect of Remifentanil on Ventilation during Normoxia and Hyperoxia



Niesters et al., Br. J. Anaesth, 2013

Previous Estimates of Respiratory Depression
(Intermittent Assessment)

Table 1 Reported incidence of respiratory depression as indicated by ventilatory frequency lower than predetermined value

	Number of study groups	Total number of patients	Respiratory depression	
			Mean (%)	95% CI
Analgesic technique				
All	116	29 607	1.1	0.7–1.7%
I.M.	10	1590	0.8	0.2–2.5%
I.V.-PCA	35	6922	1.2	0.7–1.9%
Epidural	71	21 035	1.1	0.6–1.9%

Table 2 Reported incidence of respiratory depression as indicated by oxygen saturation below predetermined value

	Number of study groups	Total number of patients	Respiratory depression	
			Mean (%)	95% CI
Analgesic technique				
All	32	1516	17.0	10.2–26.9%
I.M.	9	246	37.0	22.6–45.9%
I.V.-PCA	11	707	11.5	5.6–22.0%
Epidural	12	563	15.1	5.6–34.8%

Cashman et al. Br J Anaesth. 2004

Incidence of Respiratory Depression
(Measured Continuously)

Incidence of bradypnea

Respiratory rate less than 10 br/min

lasting for greater than 2 minutes: 58%

Incidence of hypoxia

Saturations below 90%: 21%

Overdyk et al., Anesth Analg. 2007

Incidence of Respiratory Depression
(Measured Continuously)

Incidence of bradypnea

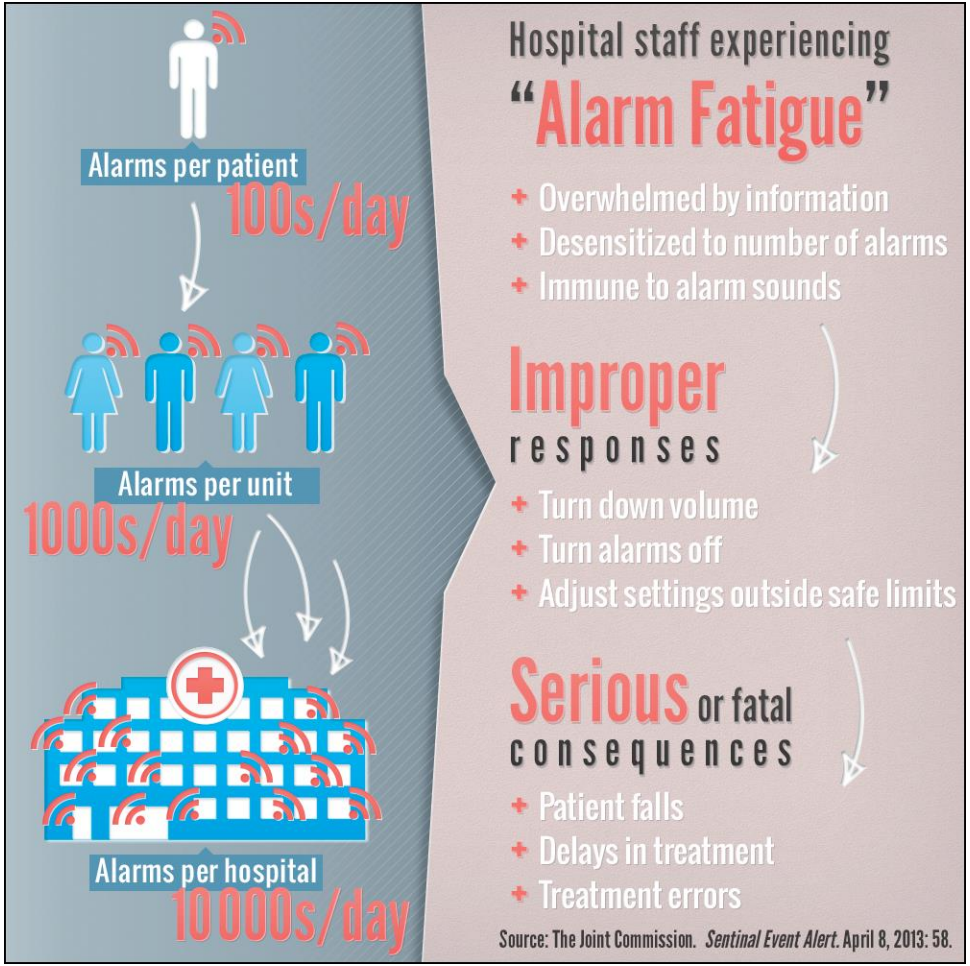
Respiratory rate less than 10 br/min

lasting for greater than 2 minutes: 58% (1.2%)

Incidence of hypoxia

Saturations below 90%: 21% (11.5%)

Overdyk et al., Anesth Analg. 2007



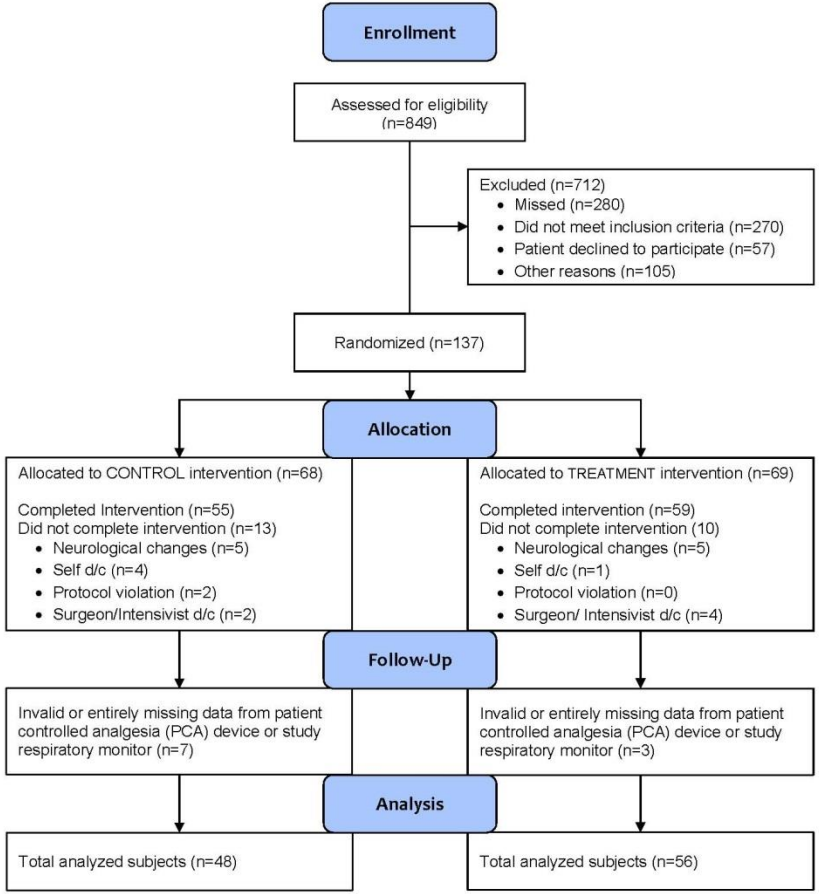
Mitka. JAMA. 2015

PCA-SAME Study: Post Craniotomy Analgesia-Safety Monitoring with EtCO2

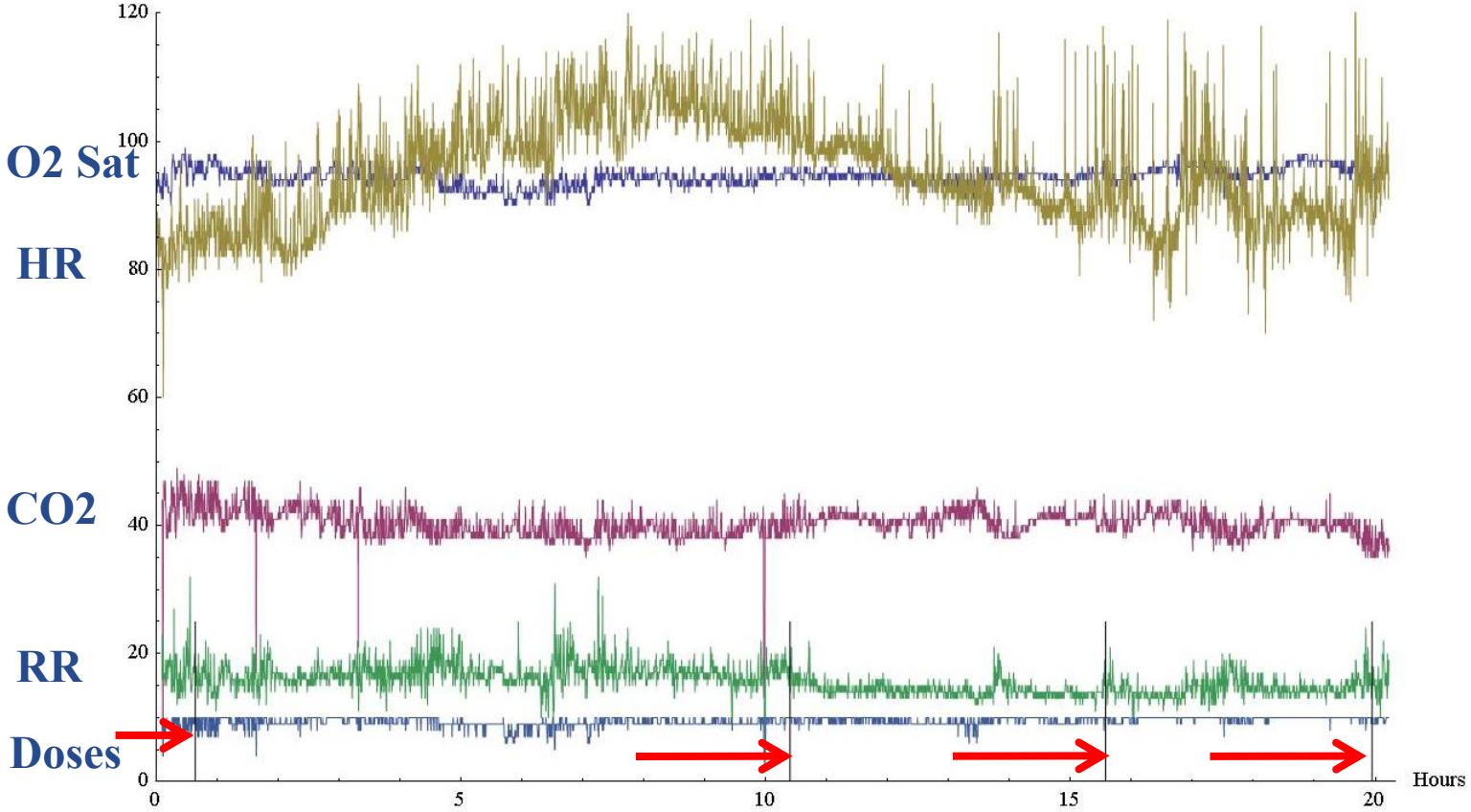
Primary Objective:

To determine the safety of opioid analgesic therapy in male and female adult post- supratentorial craniotomy patients randomly assigned to receive either IVPCA or IV PRN opioids as defined by

Respiratory rate < 10 breaths per minute [bpm] for greater than 2 minutes measured non-invasively by side stream capnography.

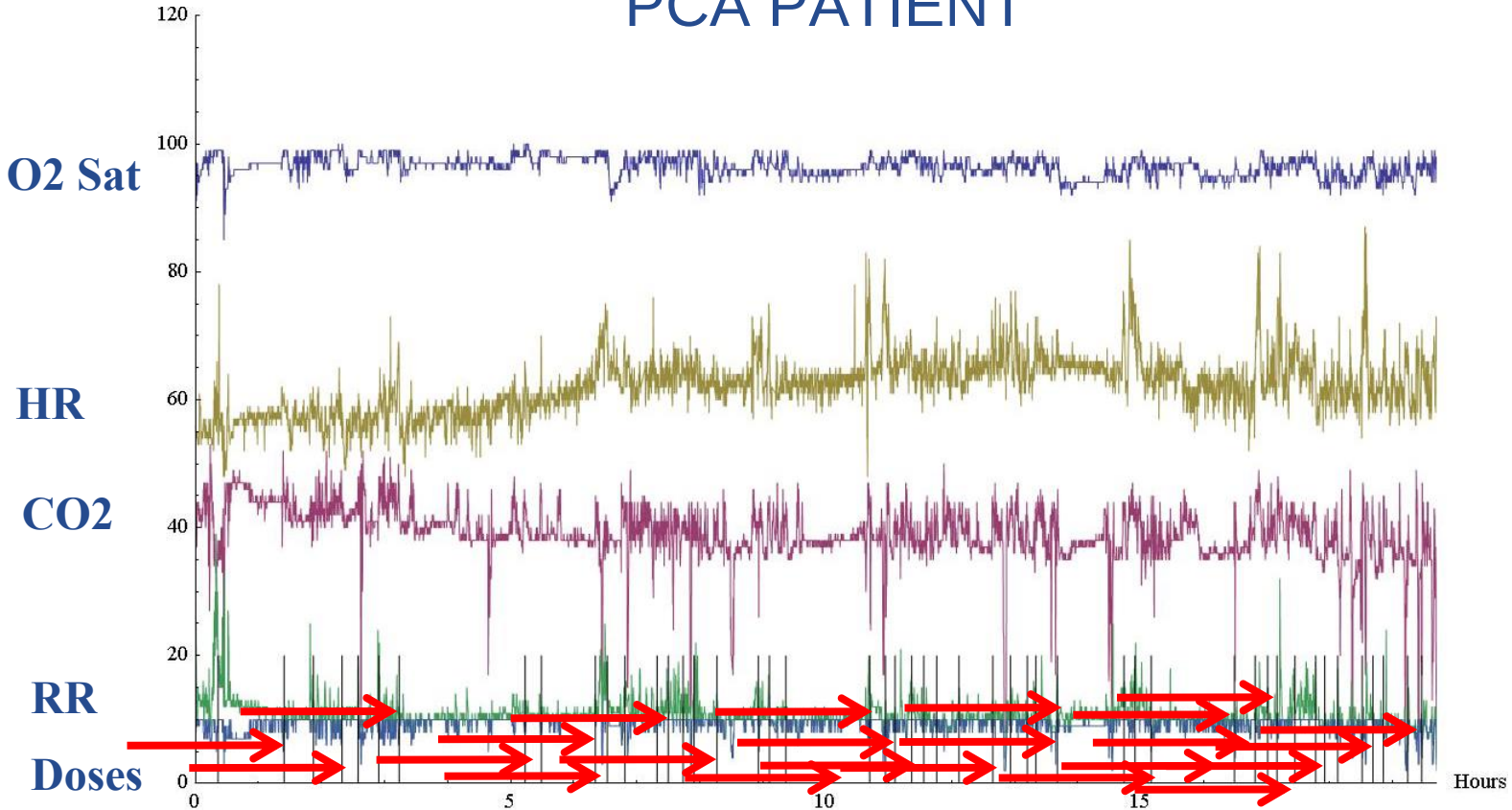

Enrollment
Assessed for eligibility (n=849)
Excluded (n=712)
• Missed (n=280)
• Did not meet inclusion criteria (n=270)
• Patient declined to participate (n=57)
• Other reasons (n=105)
Randomized (n=137)
Allocation
Allocated to CONTROL intervention (n=68)
Completed Intervention (n=55)
Did not complete intervention (n=13)
• Neurological changes (n=5)
• Self d/c (n=4)
• Protocol violation (n=2)
• Surgeon/Intensivist d/c (n=2)
Allocated to TREATMENT intervention (n=69)
Completed intervention (n=59)
Did not complete intervention (10)
• Neurological changes (n=5)
• Self d/c (n=1)
• Protocol violation (n=0)
• Surgeon/ Intensivist d/c (n=4)
Follow-Up
Invalid or entirely missing data from patient controlled analgesia (PCA) device or study respiratory monitor (n=7)
Invalid or entirely missing data from patient controlled analgesia (PCA) device or study respiratory monitor (n=3)
Analysis
Total analyzed subjects (n=48)
Total analyzed subjects (n=56)

PRN PATIENT



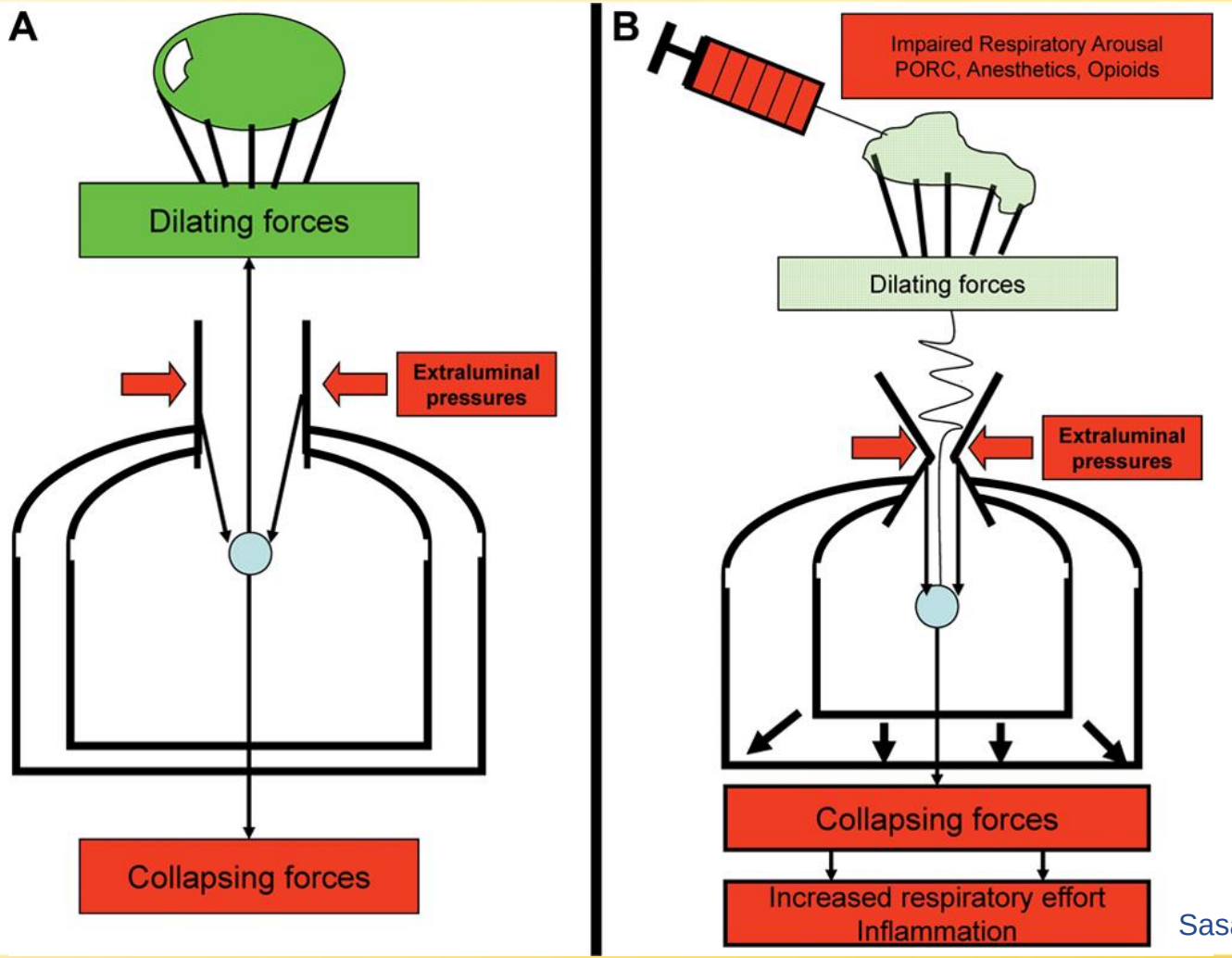
Morad et al., American Society of Anesthesiologists. 2015

PCA PATIENT



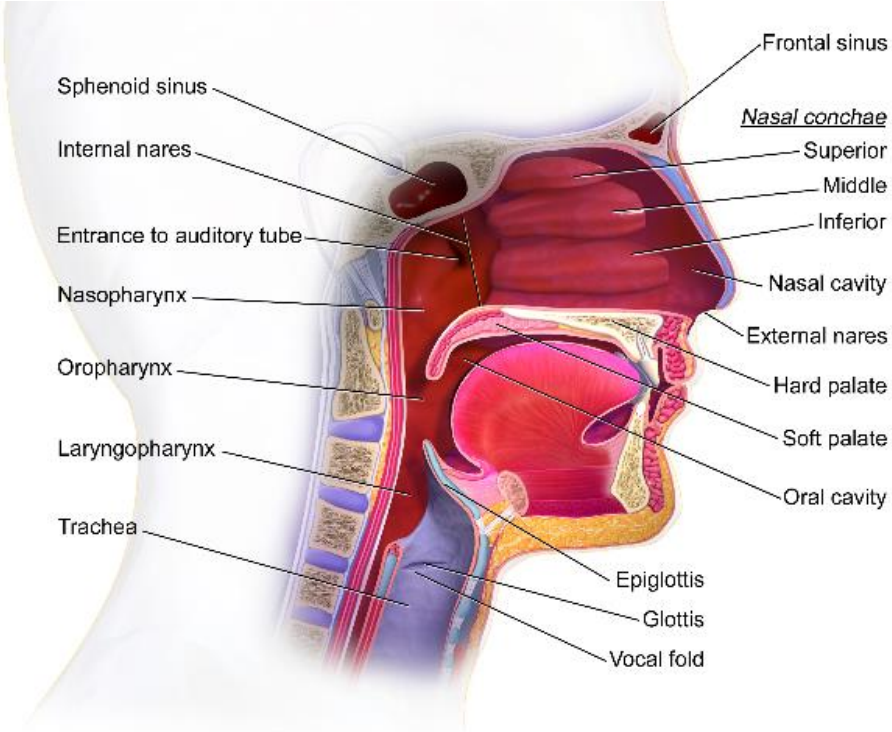
Morad et al., American Society of Anesthesiologists. 2015

Morad et al., American Society of Anesthesiologists. 2015

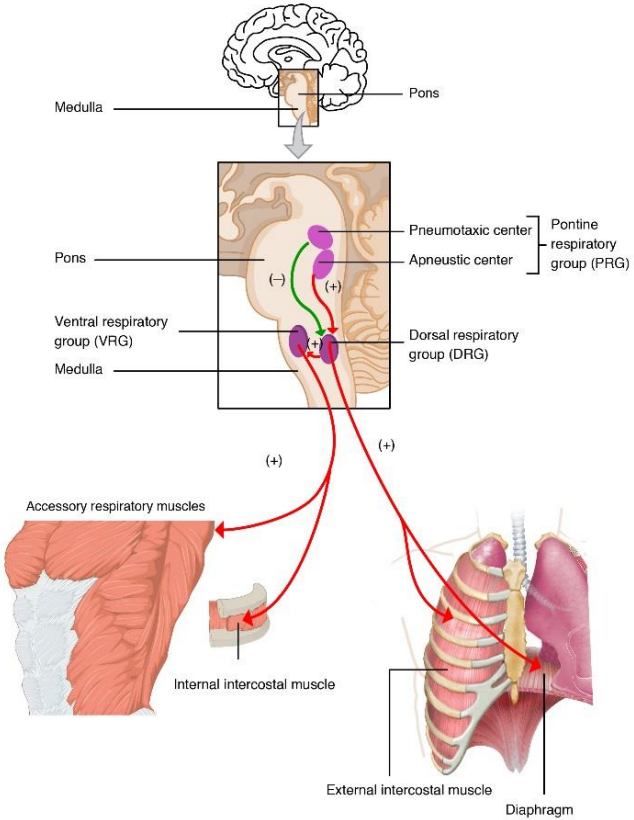


Sasaki et al., Anesthesiology. 2013

Effect of Opioids on Breathing



The Upper Respiratory System



Post Test

Opioids can induce respiratory depression.

Post Test

Pulse oximetry reliably captures episodes of respiratory depression in patients recovering from ophthalmologic surgery.

Post Test

Respiratory depression increases measured End Tidal CO2.

Post Test

End Tidal CO2 measurement provides reliable detection of opioid induced respiratory depression.

Summary

1. Opioids, alone and in combination with other sedatives, induce respiratory depression by decreasing respiratory drive AND obstructing upper airway motor tone.
2. Continuous monitoring for respiratory depression is better than intermittent assessment.
3. Supplemental oxygen masks opioid induced respiratory depression.
4. End-tidal CO2 monitoring in non-intubated patients is inadequate in detecting opioid induced respiratory depression.
5. Preoperative patient screening and postop monitoring protocols are critically important.

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