Drug-induced neuro-respiratory alterations useful for physiotherapists

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No conflict of interest to declare

True or false?

1- There is an excellent parallelism between the coma Glasgow score and the gag reflex suppression in a patient with suspected drug-induced coma.

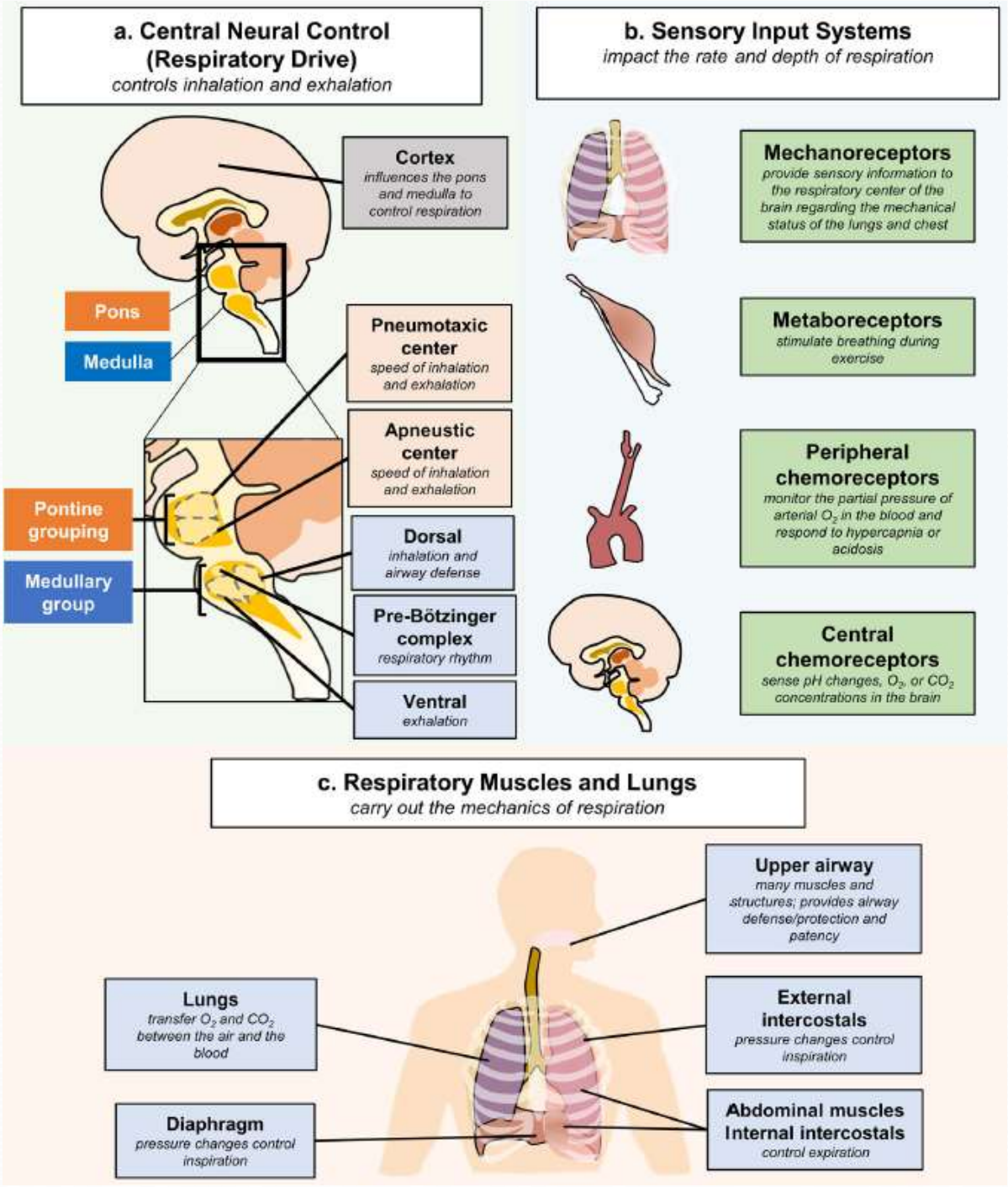
2- The right basal site of aspiration pneumonia is the most common regardless of the comatose patient's position.

3- SpO_2 is a better surrogate marker of respiratory depression than $PaCO_2$.

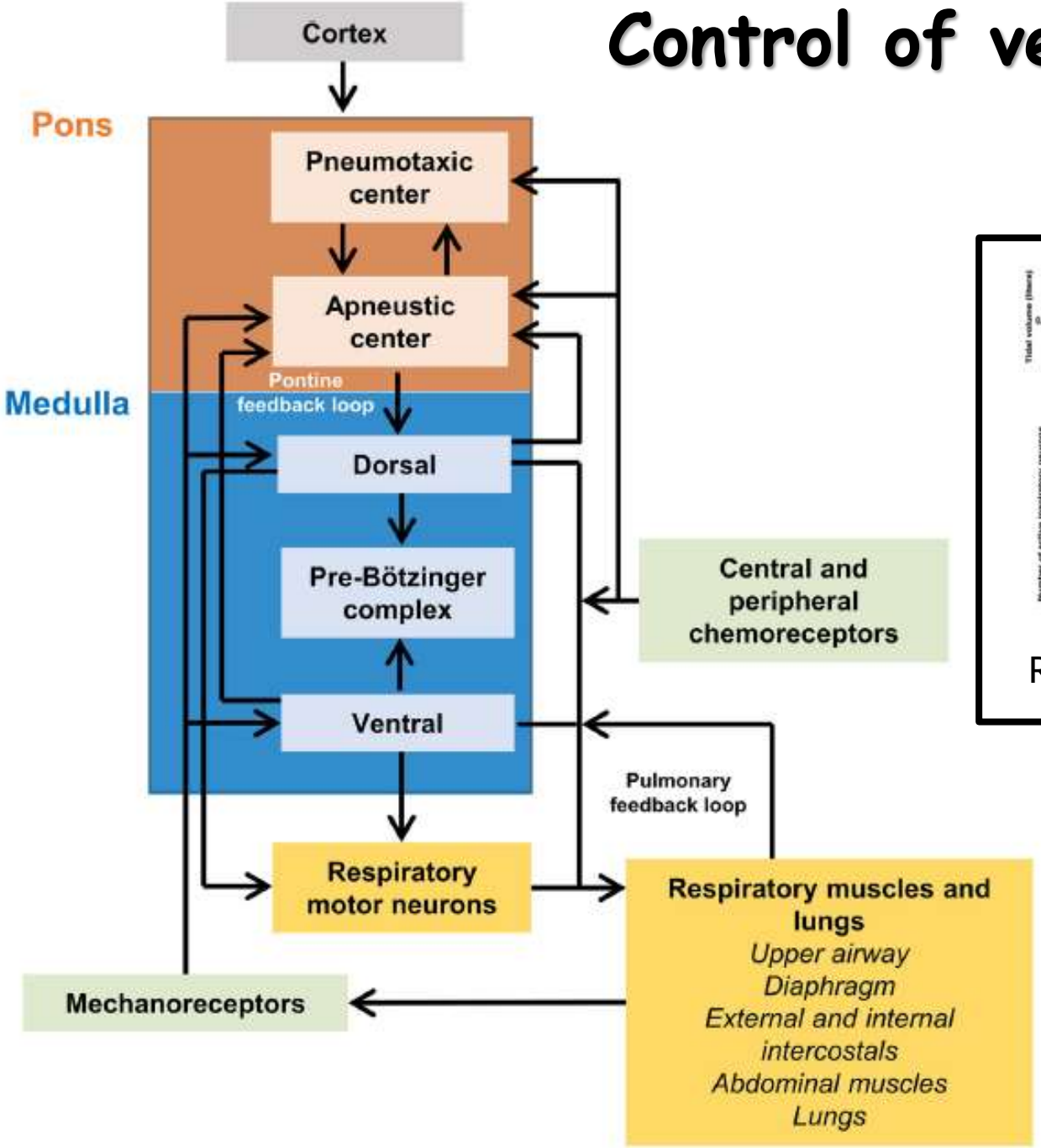
4- Benzodiazepines are mainly responsible for a CNS respiratory depression.

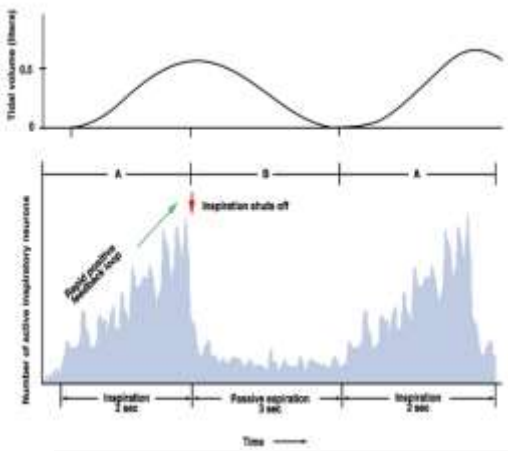
5- Naloxone administration is at risk and systematically requires a medical prescription in a comatose patient with suspected opioid overdose.

The three components of respiration



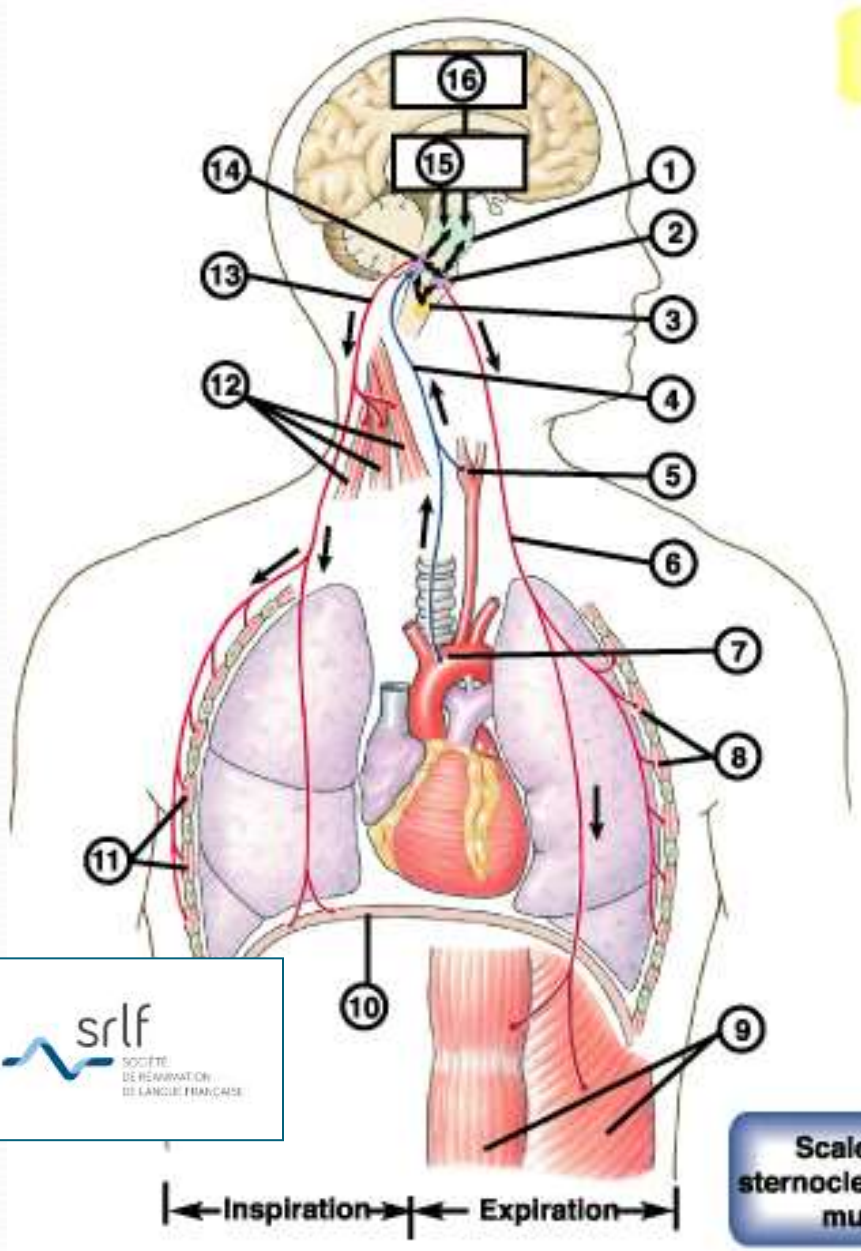
Control of ventilation

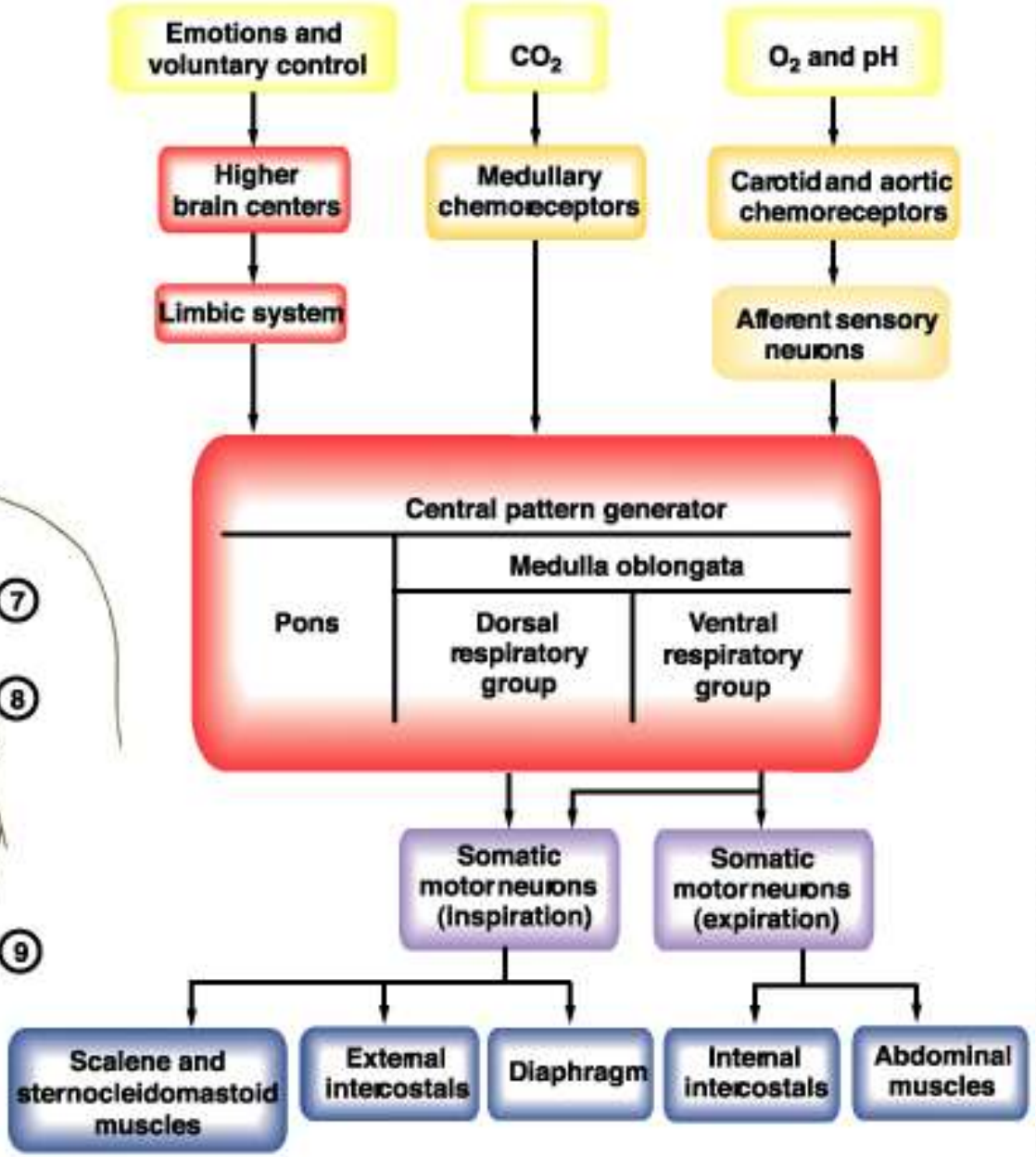




Recorded from DRG neurons

Physiological regulation of ventilation





Mechanisms of drug-induced acute respiratory failure

Type 1

Alteration of the ventilation/perfusion ratio

Hypoxemia + hypo/normocapnia

PaO_2 <8 kPa / $PaCO_2$ <6 kPa

- Aspiration pneumonia +++
- Atelectasia
- Pneumonitis (ARDS) → Direct toxicity → MOF
- Cardiogenic edema

Type 2

Alveolar hypoventilation

Hypoxemia + hypercapnia

PaO_2 <8 kPa / $PaCO_2$ >6 kPa

- Central apnea
- Obstructive apnea
- Bronchospasm
- Neuromuscular blockage

Jay SJ. Am Rev Respir Dis 1975

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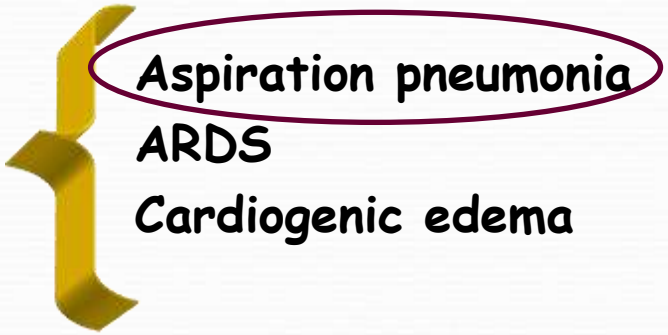
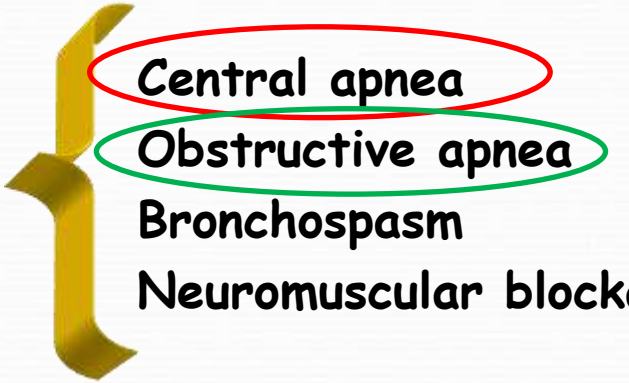
Drugs and pathophysiology of respiratory failure



All sedative drugs
Stabilisants de membrane, paraquat
Cardiotropic drugs



Opioids, barbiturates, cyanide
Benzodiazepines, ethanol
Inhaled drugs/toxicants
Muscle-paralyzing agents, anticholinesterase agents

1

Aspiration pneumonia

The non drug-specific mechanism of acute respiratory failure

Pathogenesis and risk factors for aspiration

Pathogenesis and risk factors for the development of pneumonia after macroaspiration

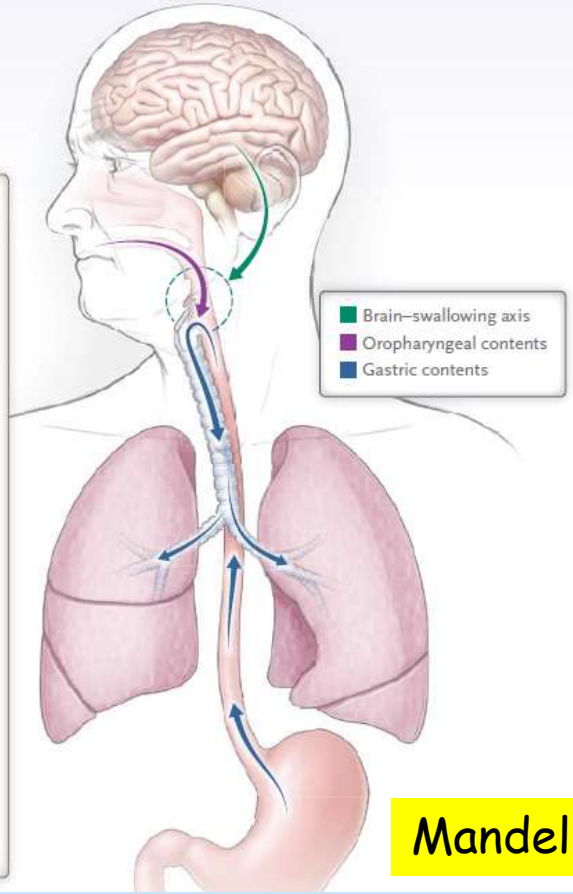
Risk Factors

Impaired swallowing
- Esophageal disease: dysphagia, cancer, stricture
- Chronic obstructive pulmonary disease
- Neurologic diseases: seizures, multiple sclerosis, parkinsonism, stroke, dementia
- Mechanical ventilation extubation

Impaired consciousness
- Neurologic disease: stroke
- Cardiac arrest
- Medications
- General anesthesia
- Alcohol consumption

Increased chance of gastric contents reaching the lung
- Reflux
- Tube feeding

Impaired cough reflex
- Medications
- Alcohol
- Stroke
- Dementia
- Degenerative neurologic disease
- Impaired consciousness



Mandell LA. *NEJM* 2019

- Defense mechanisms to prevent aspiration include strong cough reflex, active mucociliary clearance mechanism, and effective immune system.
- Aspiration results from altered swallowing due to CNS dysfunction such as coma. Oropharyngeal or gastric contents can enter the lung. Impaired cough reflex increases the likelihood that aspirated material reach the lung

Aspiration pneumonitis in an overdose population: frequency, predictors, and outcomes

Patients with aspiration pneumonitis: **1.6%** [1.2–2.0]

Higher ICU admission rate

Increased mortality: 8.5% vs. 0.4%; OR, **23** [9–60]; $p < .0001$)

Prolonged ICU stay (**126 h** [62–210] vs. 14.7 h [7–23]; $p < .0001$).

Predictor	Odds Ratio	95% Confidence Interval
Age		
10-yr increase	1.18	1.01 – 1.38
Emesis		
No (reference)	—	—
Yes	2.41	1.34 – 4.34
Ingestion to hospital presentation time		
<4 hrs (reference)	—	—
4–24 hrs	2.89	1.41 – 5.96
>24 hrs	4.64	2.45 – 8.79

Isbister GK. *Crit Care Med* 2004

Risk factors for prolonged ICU stay in self-poisoned patients

Selected parameters	Odds ratio	*p* Value
Demographics and history		
Age	1.02 (0.99; 1.04)	0.1
Psychiatric diseases	0.78 (0.38; 1.59)	0.5
Addiction	0.62 (0.31; 1.26)	0.2
Toxicants		
Psychotropic drugs	1.18 (0.53; 2.62)	0.7
Cardiotoxicants	0.68 (0.26; 1.73)	0.4
Ethanol	0.28 (0.11; 0.66)	0.005
Multidrug exposure	1.13 (0.52; 2.45)	0.8
Clinical parameters on admission		
SAPS II	1.01 (0.99; 1.03)	0.3
Glasgow coma score	0.98 (0.89; 1.06)	0.6
Complications		
Aspiration pneumonia	8.48 (4.28; 17.3)	<0.001
Cardiovascular failure[a]	1.33 (0.51; 3.43)	0.6
Cardiac contractility impairment[b]	0.64 (0.23; 1.76)	0.4
Cardiac arrest	0.15 (0.04; 0.52)	0.003
Seizures	2.49 (0.77; 8.73)	0.1
Acute kidney injury	3.15 (1.36; 7.39)	0.008
Acute liver failure	0.69 (0.25; 1.99)	0.5
Rhabdomyolysis	0.97 (0.44; 2.12)	0.9
Multiple organ failure	8.06 (3.43; 19.9)	<0.001
Outcome		
Delayed awakening[c]	8.64 (2.58; 40.7)	0.002
Management		
Veno-arterial ECMO	0.82 (0.23; 3.13)	

Naim *G. Clin Tox 2022*

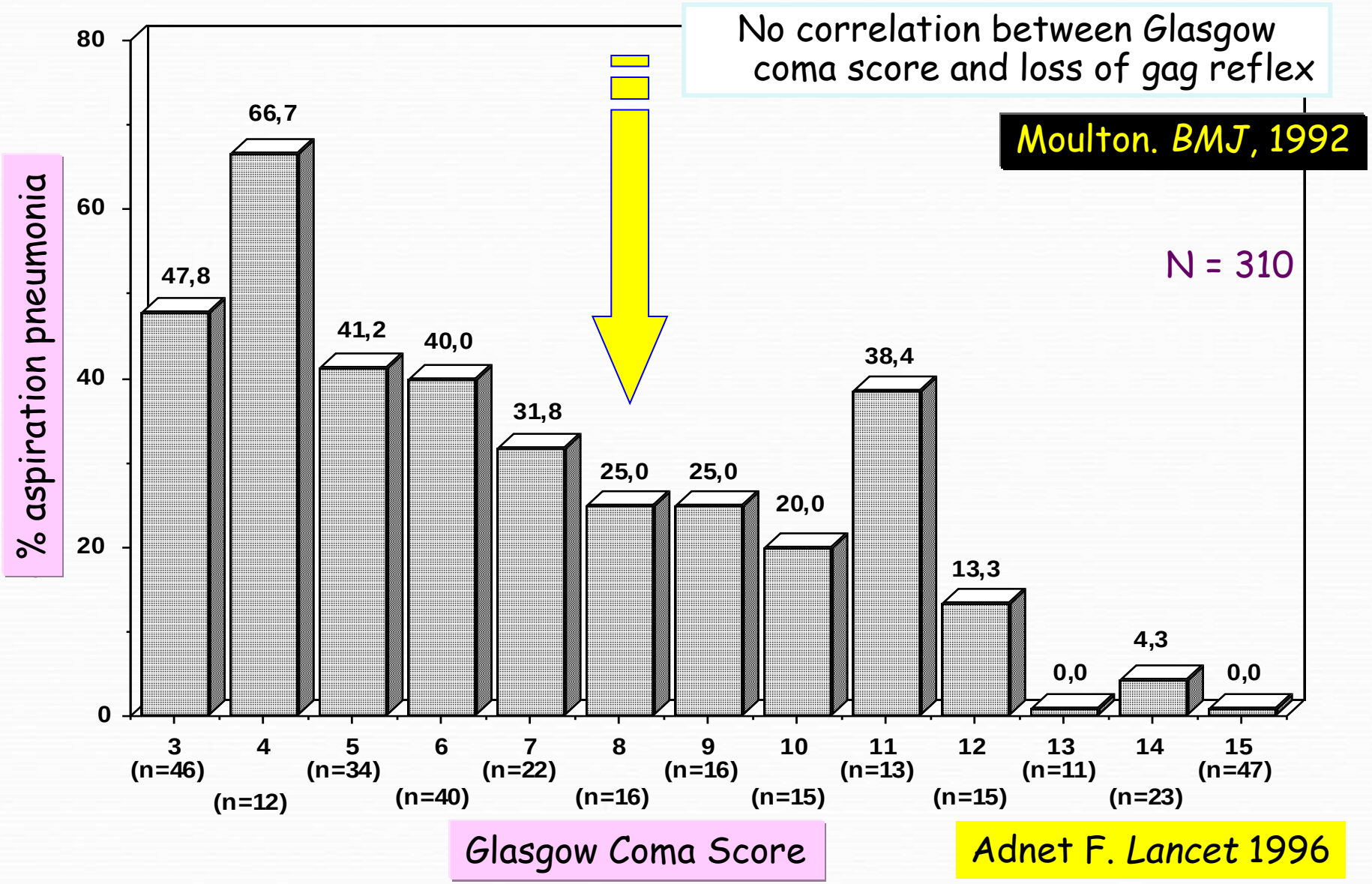
Aspiration pneumonia in the poisoned patient: necessity of early airway management

Association between aspiration pneumonia onset and delayed intubation until arrival at the ED

N=72	Patients with Aspiration Pneumonia	Patients without Aspiration Pneumonia	*p*-Value
Women	12	27	-
Men	9	24	0.75
GCS of 8 or less	15	32	0.48
Emesis	8	7	0.046
Active charcoal	3	1	0.07
Delayed intubation to ED admission in unconscious patient	9	4	0.002

Montassier E. *J Emerg Med* 2012

Glasgow coma score and risk for aspiration



Relation of body position at the time of discovery with aspiration pneumonia in the poisoned comatose patients

Position	Aspiration pneumonia	GCS
Prone (n=20)	1 (5%)*	6 ± 3
Suppine (n=115)	48 (42%)	6 ± 3
Left Lateral (n=31)	8 (26%)	6 ± 3
Right lateral (n=21)	11 (52%)	6 ± 2
Semi-recumbant (n=20)	3 (15%)*	8 ± 2$

*$p<0.01$ vs other positions; $^{\$}p<0.05$ vs other positions

Adnet F. *Crit Care Med* 1999

Relationship between the position of the body position at the time of discovery and aspiration pneumonia on chest X-Ray

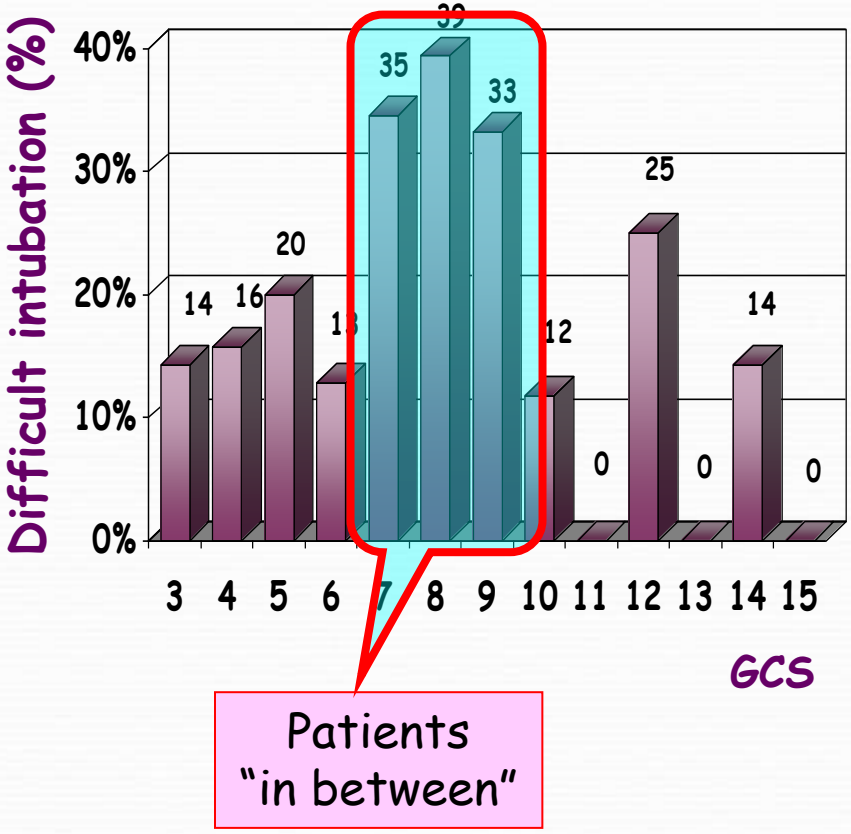
Position	Right Inf. Quadrant	Right Sup. Quadrant	Left Inf. Quadrant	Left Sup. Quadrant
Supine	69%	37%	20%	14%
Left lateral	57%	14%	29%	0%
Right lateral	80%	50%	30%	20%

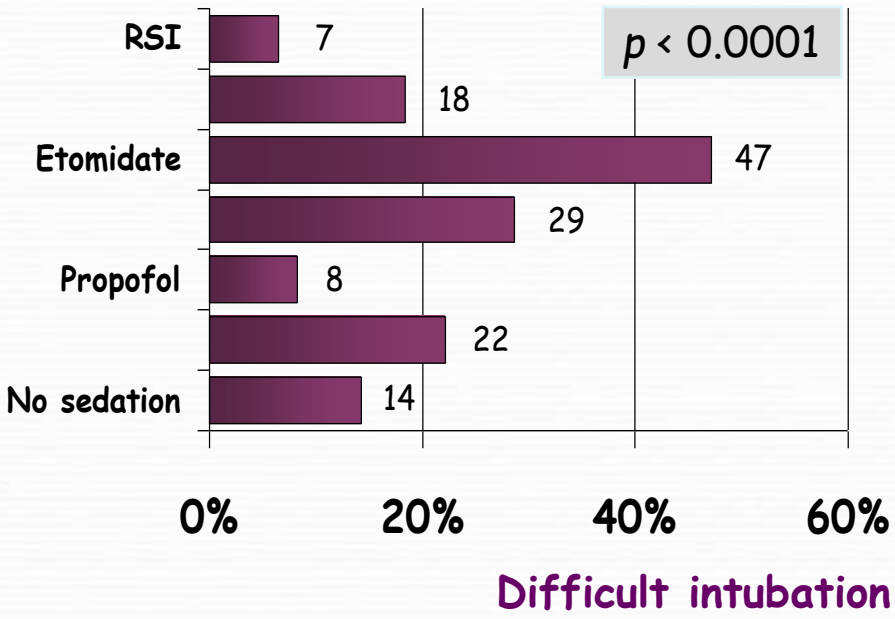
Adnet F. *Crit Care Med* 1999

Tracheal intubation difficulty in the comatose poisoned patient

Difficult intubation is frequent in the pre-hospital setting (~11%). In poisonings, it averages 20%. Choosing the best sedative drugs for anesthesia induction is highly difficult

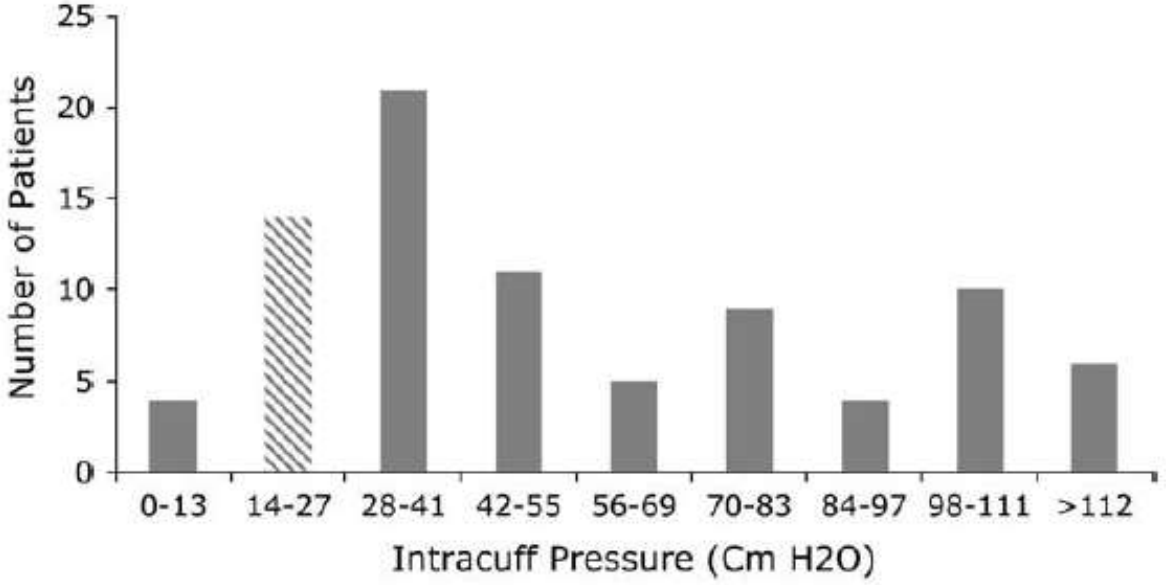
Adnet F. *Eur J Emerg Med* 1998





Adnet F. *Acad Emerg Med* 1998

Intracuff pressures of endotracheal tubes in the management of airway emergencies: an observational study



- First measurement > 27 cmH_2O in 79% patients (85/107)
- Mean value: 56 cm H_2O in the extra-hospital patients and 69 cm H_2O in the transferred patients
- A correction is required in 72% of the patients (77/107)

Galinski M. *Ann Emerg Med* 2006

Laryngeal injuries in relation to tracheal intubation

Evaluation of post-extubation laryngeal injuries in 209 poisonings

			Vocal cord		Arytenoid			
	Epiglottis	Ventricular bands	Right	Left	Right	Left	Subglottis	Number of patients (%)
Number of patients								
Normal	168	170	102	95	105	110	163	42 (20%)
With injury	41	39	107	114	104	99	46	167 (80%)
Number of separate scored lesions								
Mucosal edema	29	37	54	57	86	84	32	135 (65%)
Ulceration	11	2	38	38	14	13	10	65 (31%)
Reduced mobility	–	–	14	11	–	–	–	25 (12%)
Immobility	–	–	1	5	–	–	–	6 (3%)
Granuloma	1	–	12	10	2	–	4	14 (7%)
Subluxation	–	–	–	–	2	2	–	4 (2%)
Total[a]	41	39	119	121	104	99	46	167 (80%)

- Median duration of intubation: 24 h (13-52)
- Non-planed self-extubation : 27%

Mégarbane B. *Clin Tox* 2010

The main intubation-related laryngeal injuries

Mucosal injuries

Diffused inflammation

Cartilage subluxation

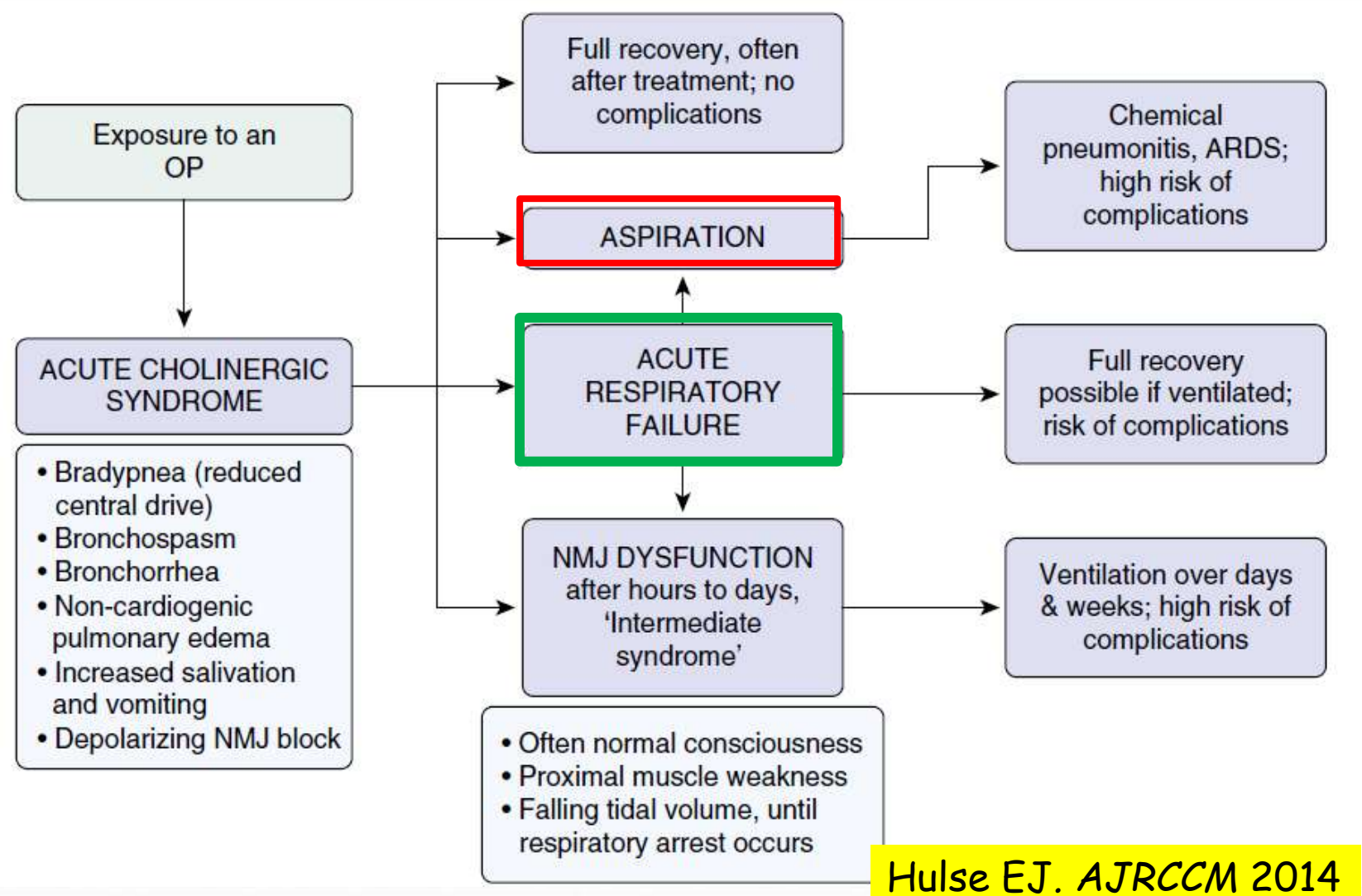
Ulcer

Vestibular fold granuloma

Tracheomalacia

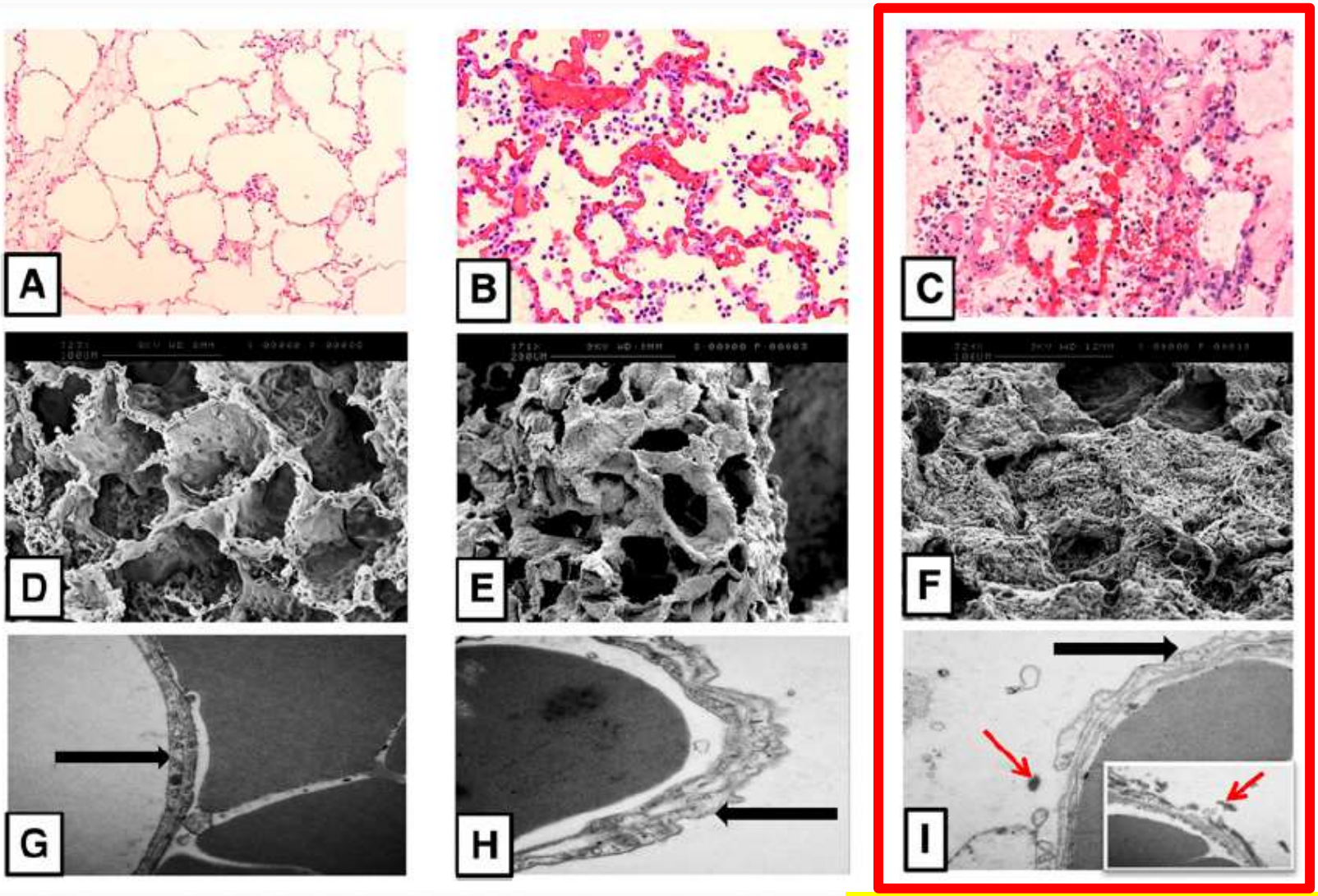
Liu J. *Anesth Analg* 2010

Respiratory system toxicity secondary to organophosphorus poisoning



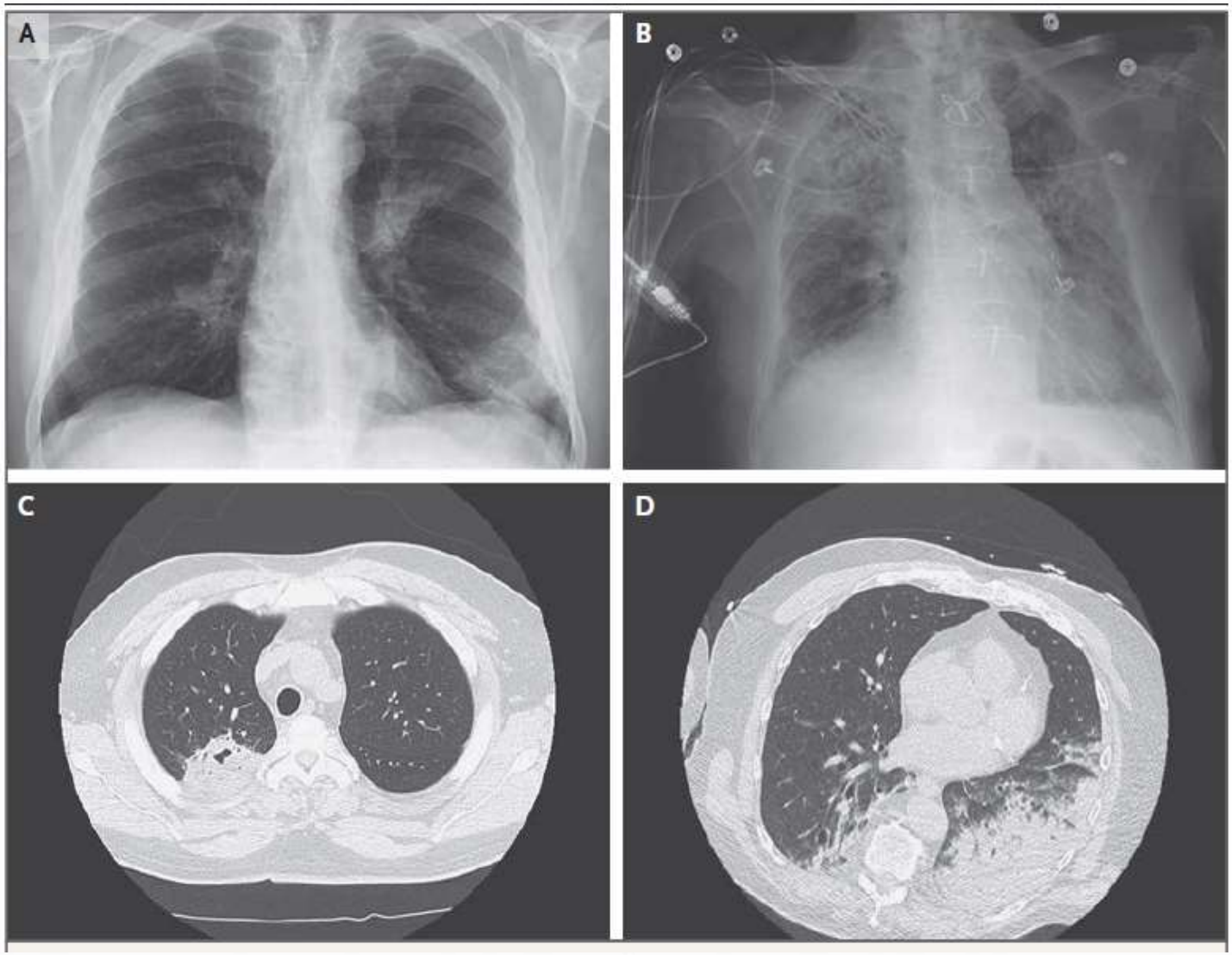
Hulse EJ. *AJRCCM* 2014

Effects of hematogenous (indirect) vs aspirated (direct) organophosphorus on minipig lung



Hulse EJ. *AJRCCM* 2014

Imaging to diagnose aspiration pneumonia



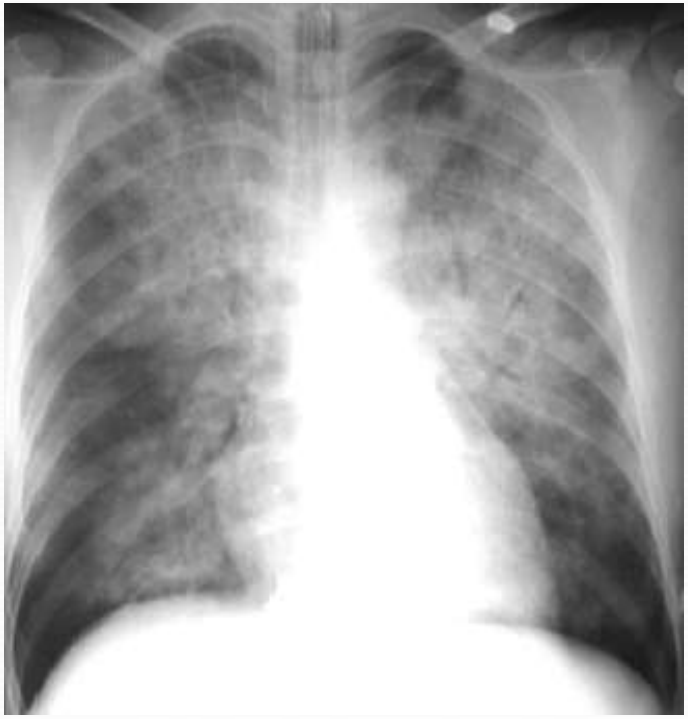
Cavitary infiltrate in the right lower lobe

Mandell LA. NEJM 2019

Cocaine-induced cardiogenic pulmonary edema

Cardiac toxicity

36-yr-old cocaine abuser woman who presented with shortness of breath and chest pain after smoking crack



Extensive bilateral heterogeneous central and parahilar opacities

Bilateral heterogeneous opacities

Restrepo CS. *Radiographics* 2007

Crack lung

Acute syndrome after the inhalation of (free base) cocaine
Presentation: Fever, hypoxemia, hemoptysis, respiratory failure

Opacities with peripheral distribution

Extensive bilateral ground-glass opacities and airspace consolidation.

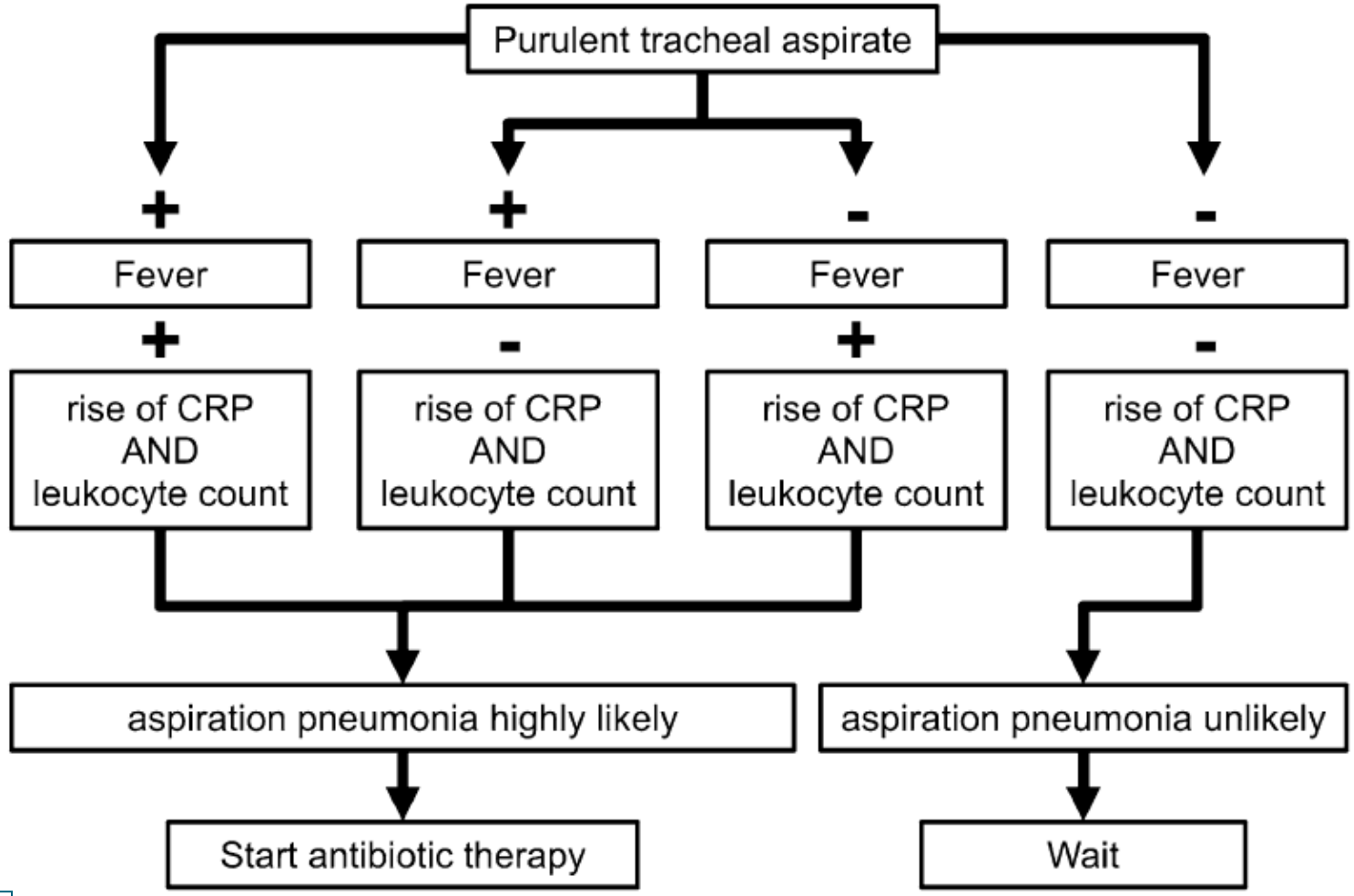
Suggested mechanisms: high temperature of volatilized drug, impurities, local vasoconstriction, macrophage activation

Restrepo CS. *Radiographics* 2007

ASPIRATION PNEUMONIA

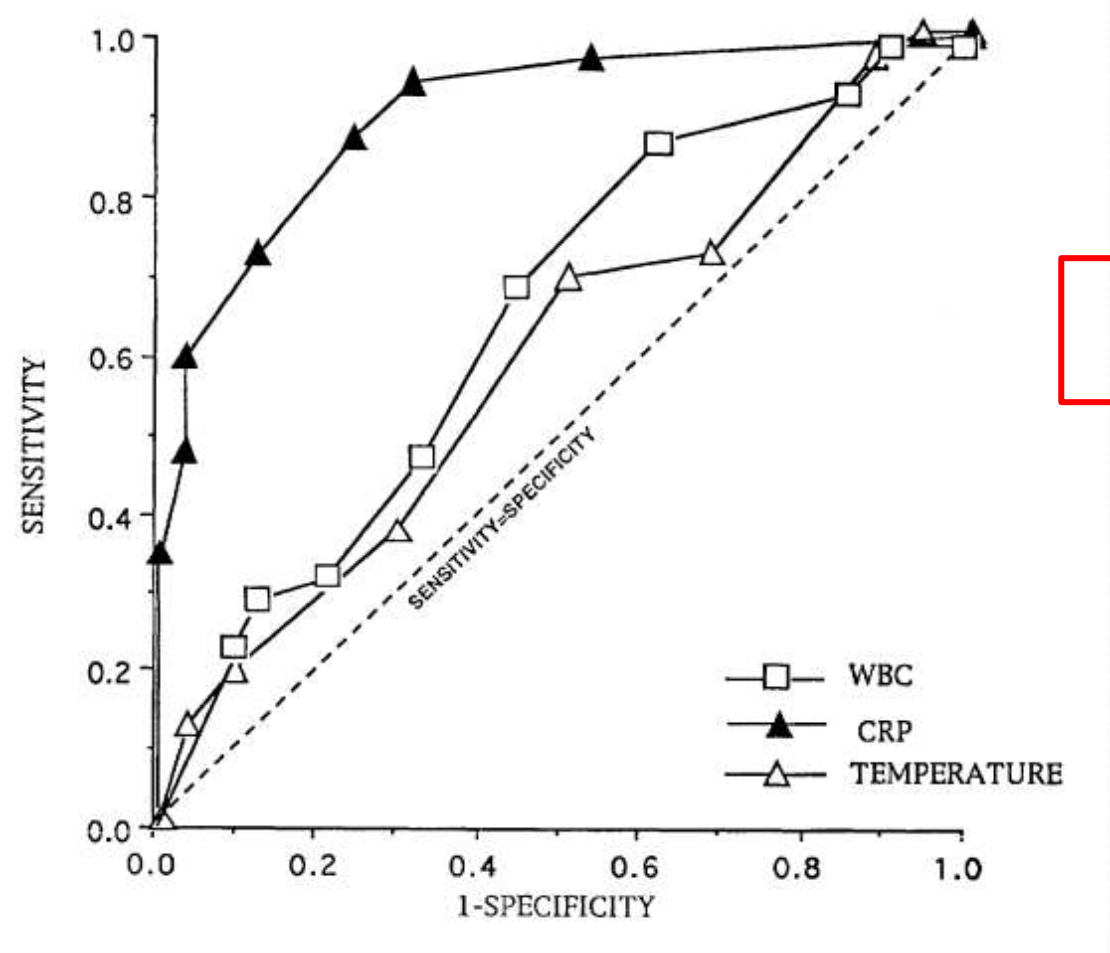
ASPIRATION PNEUMONITIS

Suspicion of aspiration pneumonia in the comatose poisoned patient



Lauterbach E. *Intern Emerg Med* 2014

Value of CRP in the detection of bacterial contamination at the time of presentation in drug-induced aspiration pneumonia



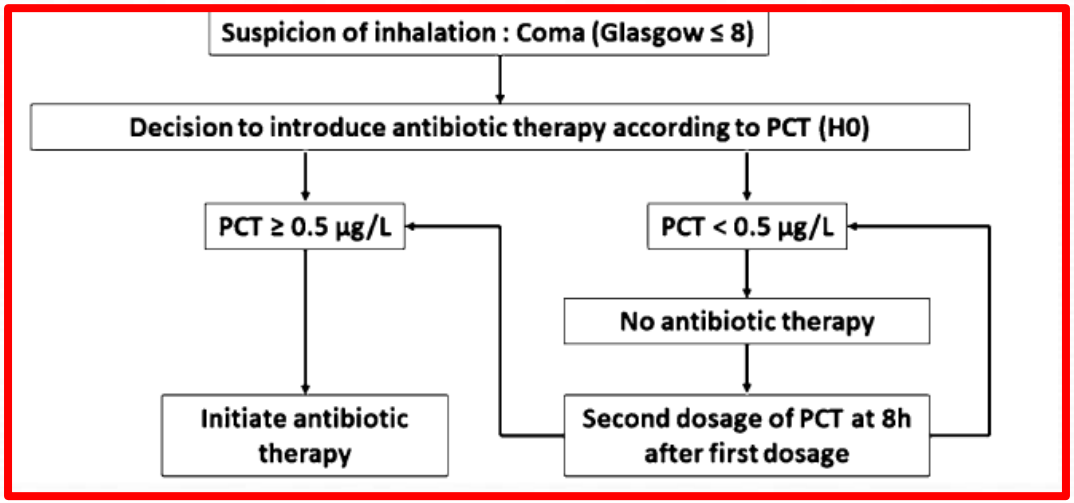
CRP >75 mg/L is associated with aerobic bacterial content of aspiration pneumonia (Se=87%, Spe=76%, PPV=78%, NPV=87%).

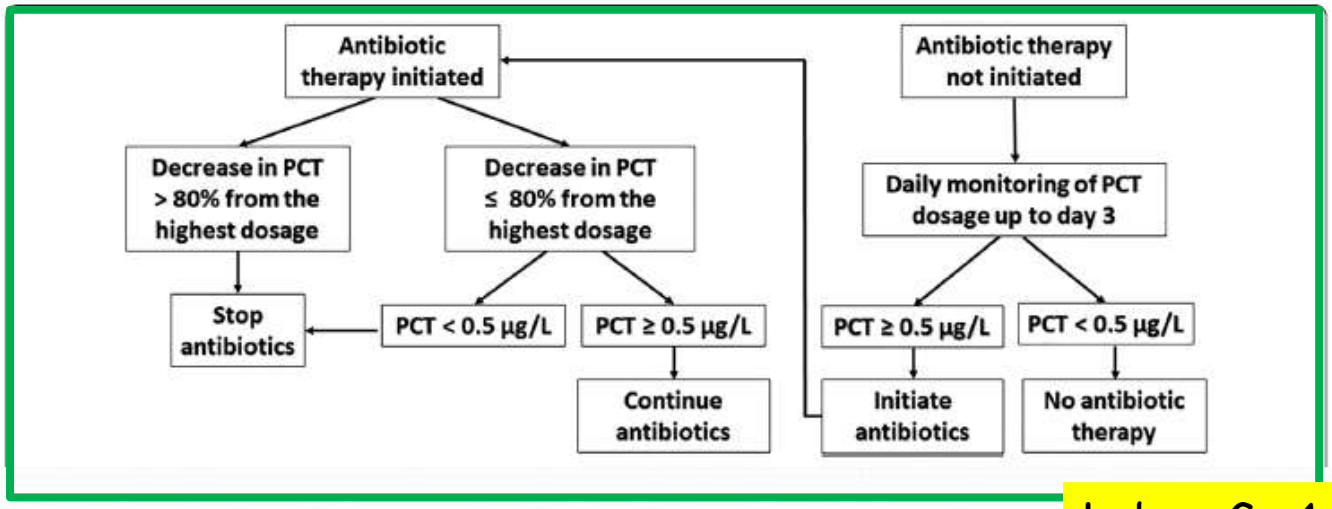
By contrast to temperature and WBC, early CRP measurement is useful for diagnosis and perhaps in determining the need for invasive sampling.

Adnet F. *Chest* 1997

Impact on antimicrobial consumption of PCT-guided antibiotics for aspiration pneumonia in comatose ventilated patients: a randomized controlled study

RCT





PCT to guide therapy vs. clinical, biological and radiological criteria, does not modify exposure to antibiotics in comatose intubated patients

Labro G. *Ann Intensive Care* 2004

Antibiotic therapy in ventilated comatose patients following aspiration: differentiating pneumonia from pneumonitis

Prospective cohort study

- Among ventilated comatose patients, those without clinical, laboratory, or radiologic evidence of bacterial aspiration pneumonia did not require antibiotics.

- In those with suspected bacterial aspiration pneumonia, stopping empirical antibiotic therapy when routine telescopic plugged catheter sampling recovered no microorganisms was nearly always effective.

- This strategy may be a valid alternative to routine full-course antibiotic therapy. Only half the patients with suspected bacterial aspiration pneumonia had confirmed diagnosis.

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Lascarrou JB. *Crit Care Med* 2017

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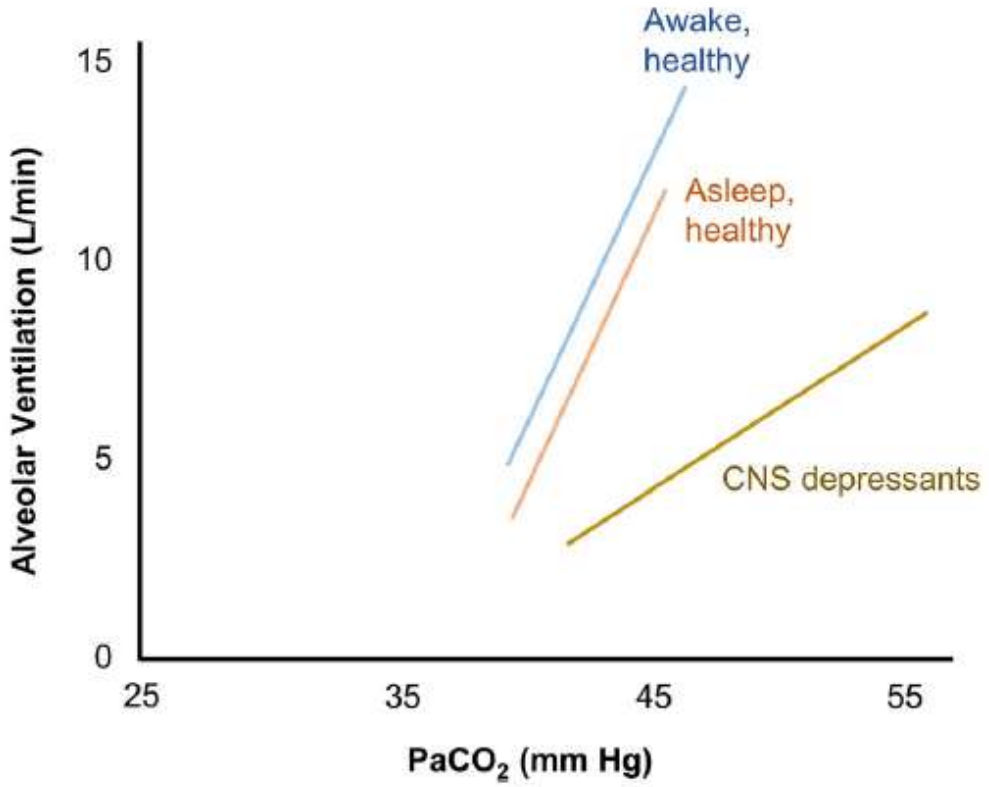
Central respiratory depression

Effect of CNS depressant exposure on the CO_2 response curve

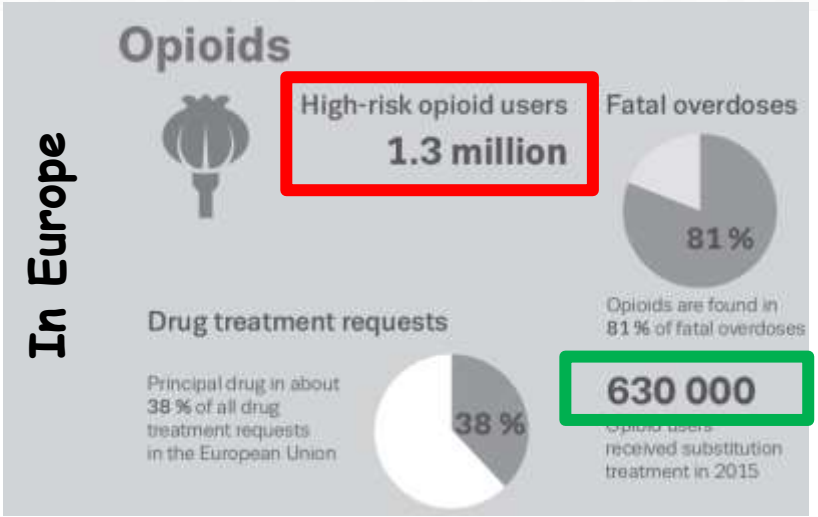


Pharmaceuticals and recreational depressant drugs can suppress one or more steps in respiration and patency.

Common depressors are opioids and barbiturates, >> benzodiazepines, Z drugs, and ethanol.

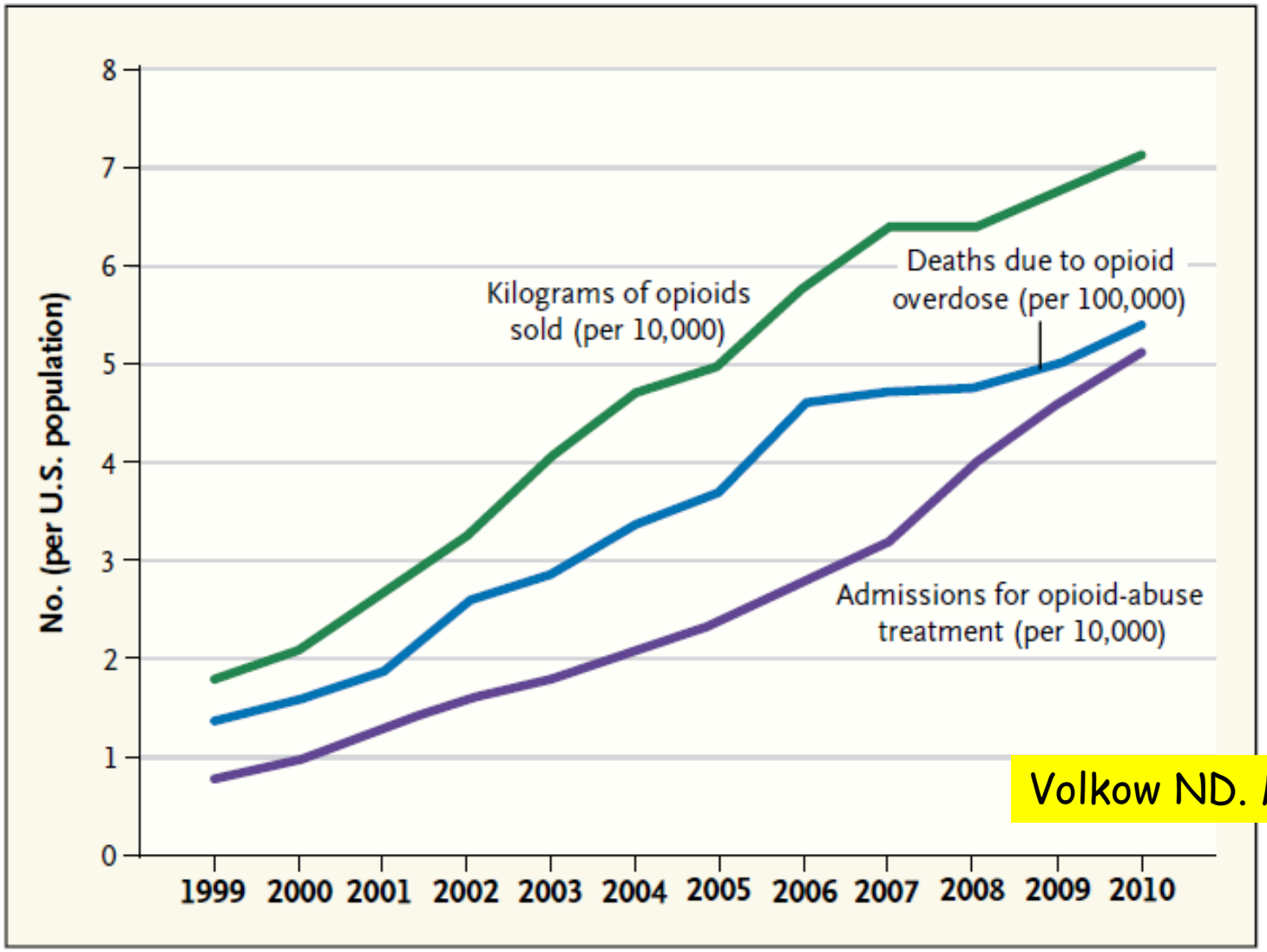
Webster LR. *Pain Ther* 2020

Opioids : the first cause of toxic death



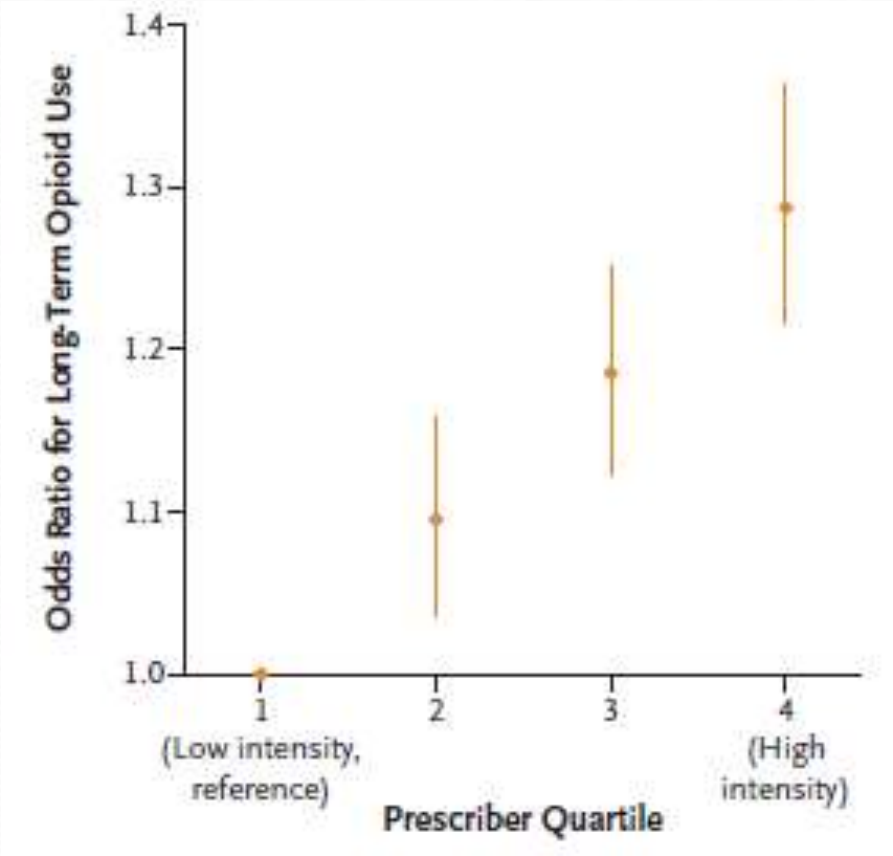
Jones CM. JAMA 2013

The US Opioid-Overdose Epidemic
Opioid sales, admissions for opioid-abuse treatment and deaths due to opioid overdose, 1999–2010



Volkow ND. *NEJM* 2014

Opioid-prescribing patterns of emergency physicians and risk of long-term use



- Rates of opioid prescribing varies widely between low-intensity and high-intensity prescribers (7.3% vs. 24.1%).

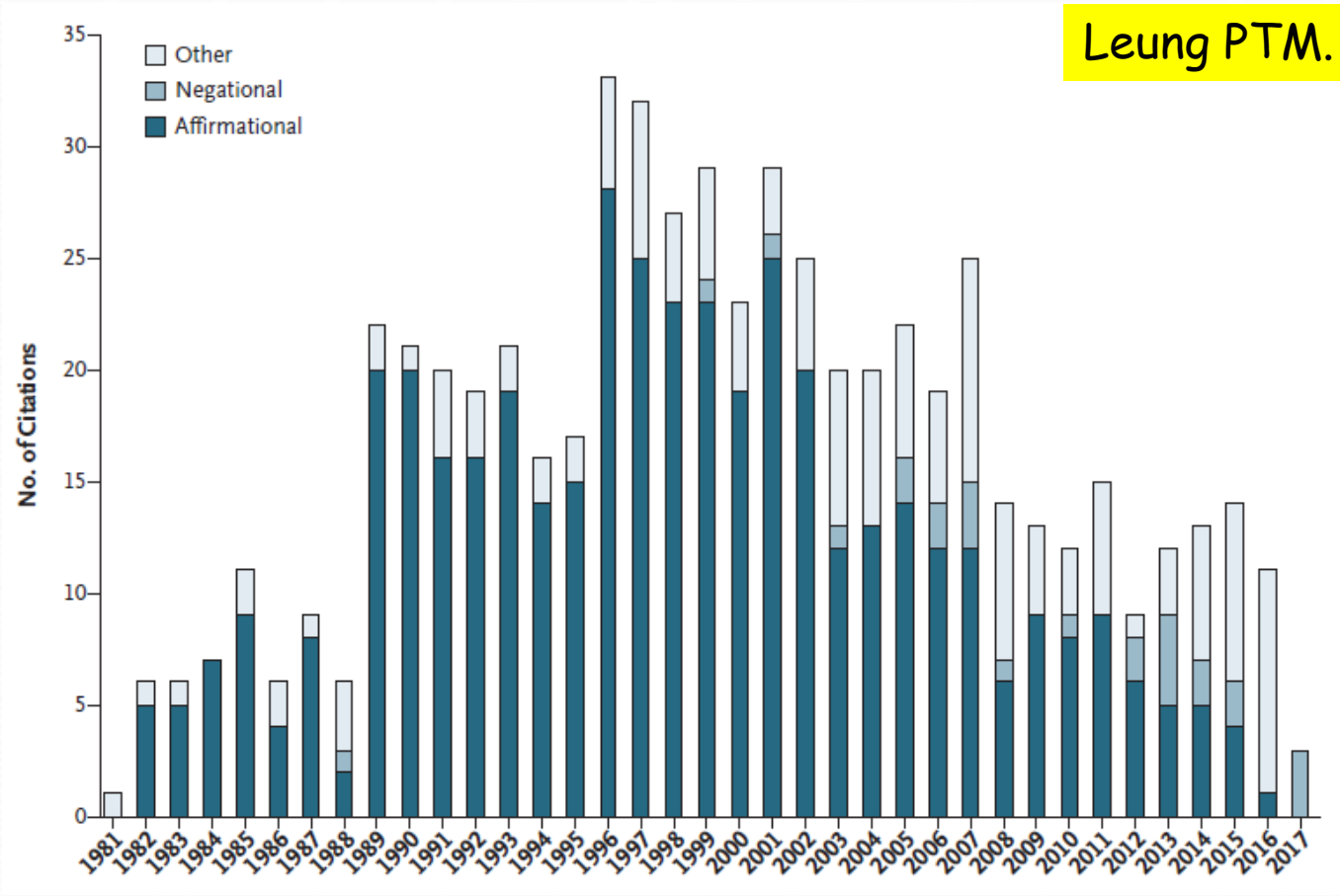
- Long-term opioid use is higher among patients treated by high-intensity prescribers than among patients treated by low-intensity prescribers (adjusted OR, 1.30 [1.23 to 1.37]; P<0.001)

Barnett ML. NEJM 2017

A 1980 NEJM letter on the risk of opioid addiction when prescribed for chronic pain

A 5-sentence letter published in the NEJM in 1980 was uncritically cited as evidence that addiction was rare with long-term opioid therapy [439/608 (72%)]

Leung PTM. NEJM 2017

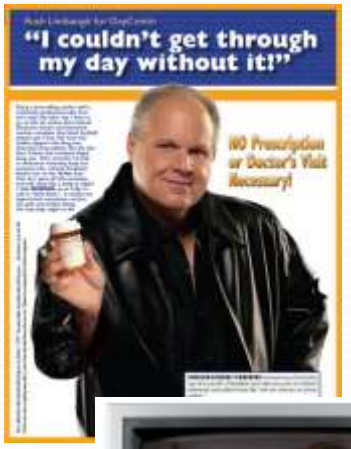


Porter J, Jick H. Addiction rare in patients treated with narcotics. NEJM 1980;302:123

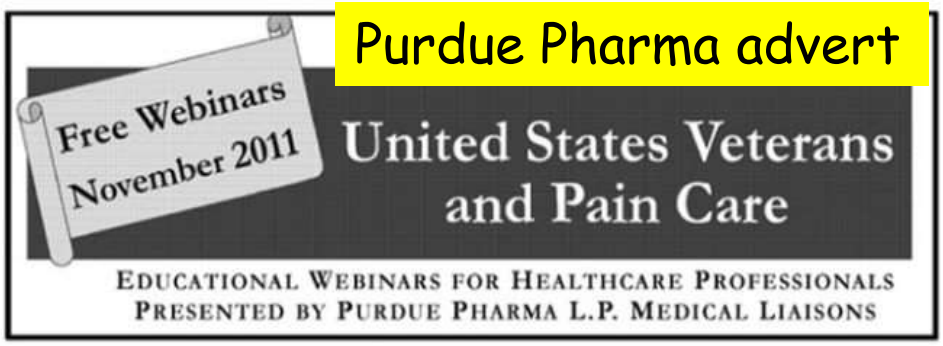
The role of Big Pharma:
Accused of causing ½ million deaths

Sackler Family

The 19th wealthiest family in the US with a fortune of $13 billion in 2016

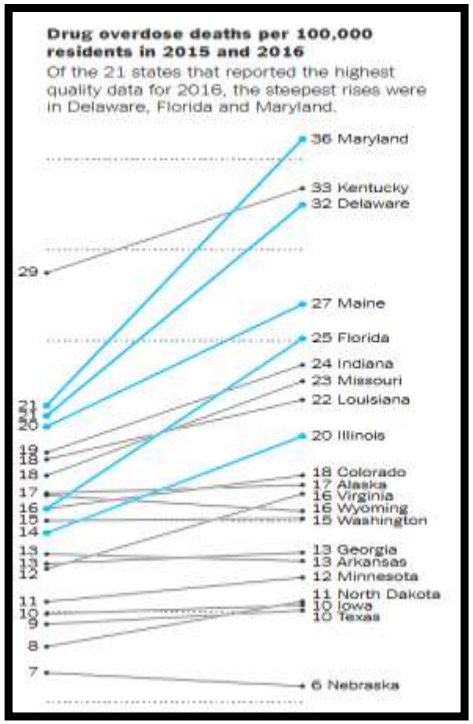


Purdue Pharma advert



Opioid-related deaths in the US (2000-2022)

~ 64,000 deaths / year



Fentanyl

Heroin

Prescription analgesics

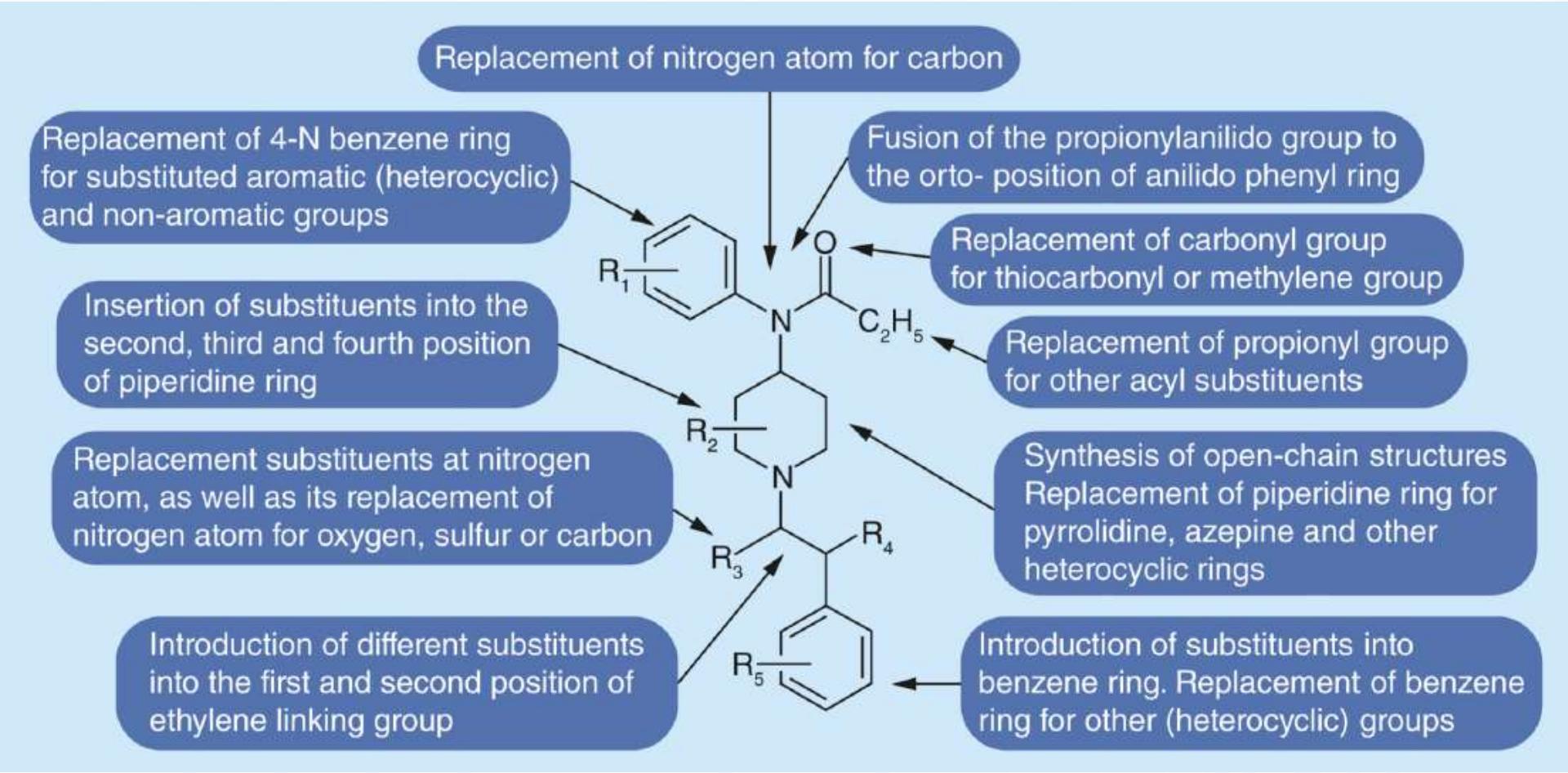
Cocaine

Methamph

Methadone

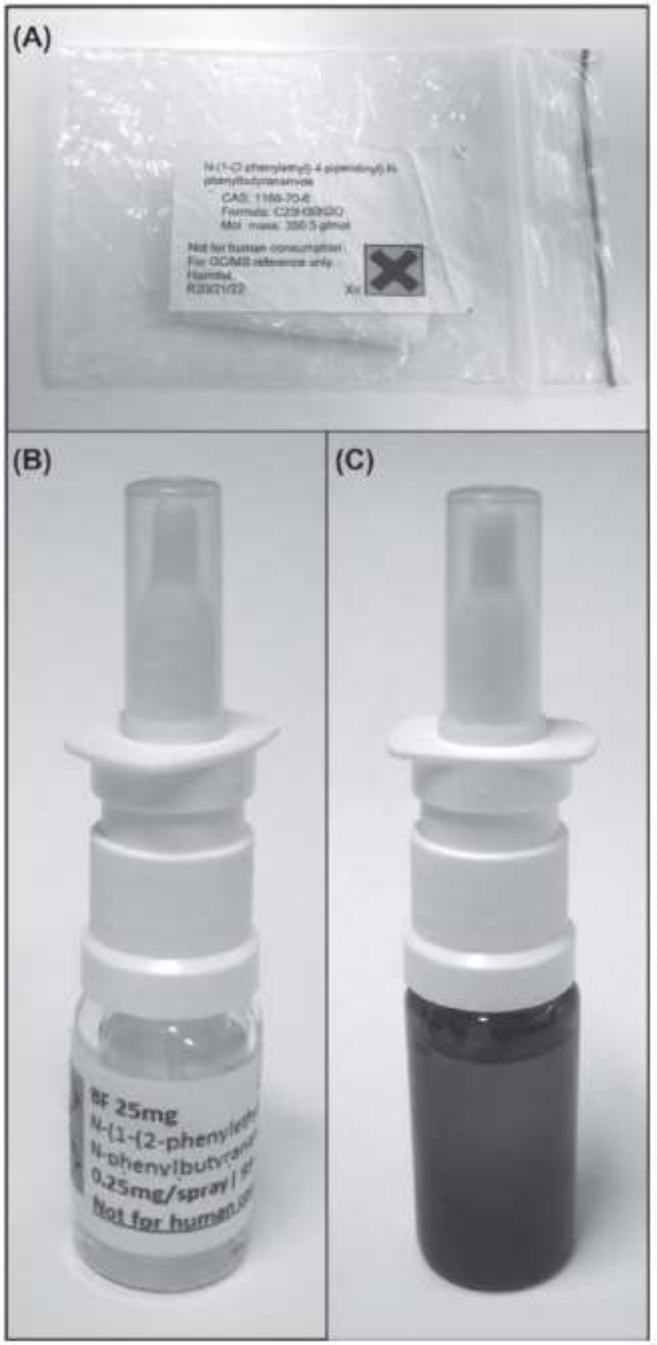
New York Times 2017

Chemistry of fentanyl derivatives



Presentation of illicitly produced designer fentanyls

25 mg butyrfentanyl labeled bottles, each spray yields 0.25 mg and the content is sufficient for 95-105 puffs.



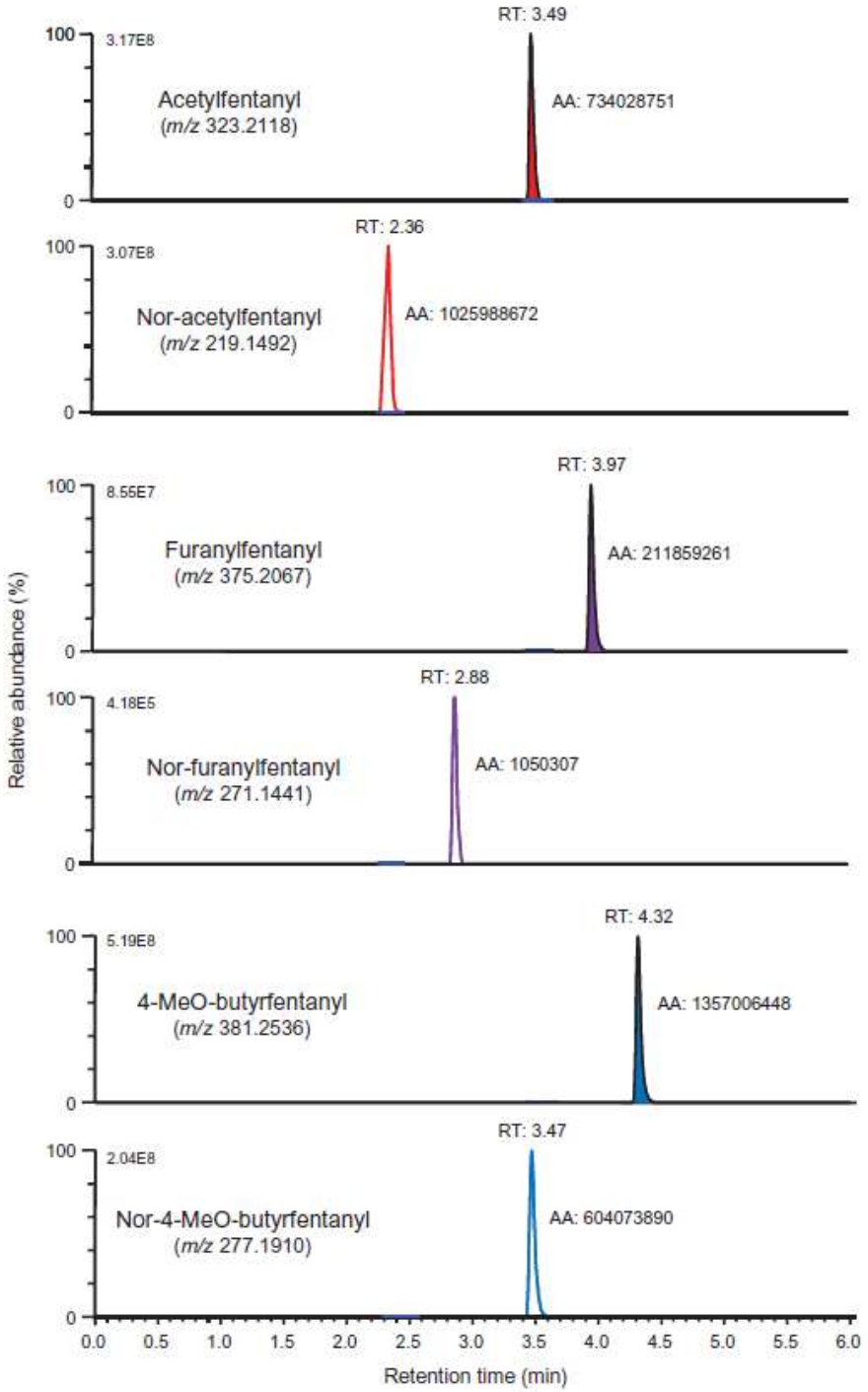
The usual presentation of opioid overdose

All opioids produce a similar toxidrome in excessive dosing.

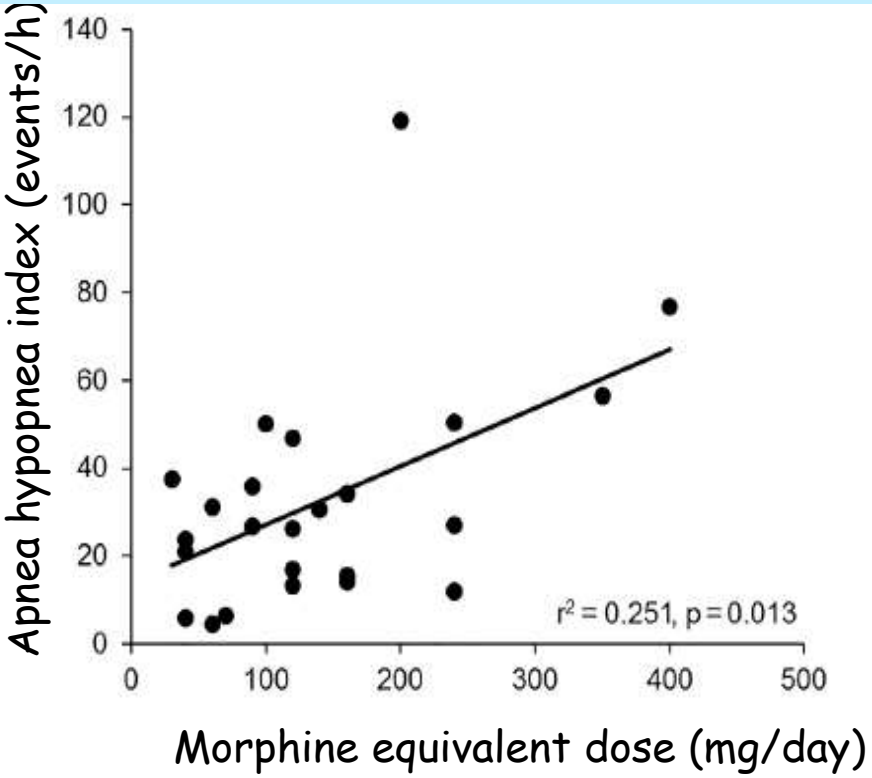
SpO_2 and RR are surrogate indicators of ventilatory drive but provide limited information on drug-related effects on ventilatory control

$PaCO_2$ and V_M are direct measures of ventilation but difficult to assess continuously

Identification by analytical techniques combining liquid chromatography + mass spectrometry (LC–HRMS, LC–MS/MS, LC–HRMS/MS)

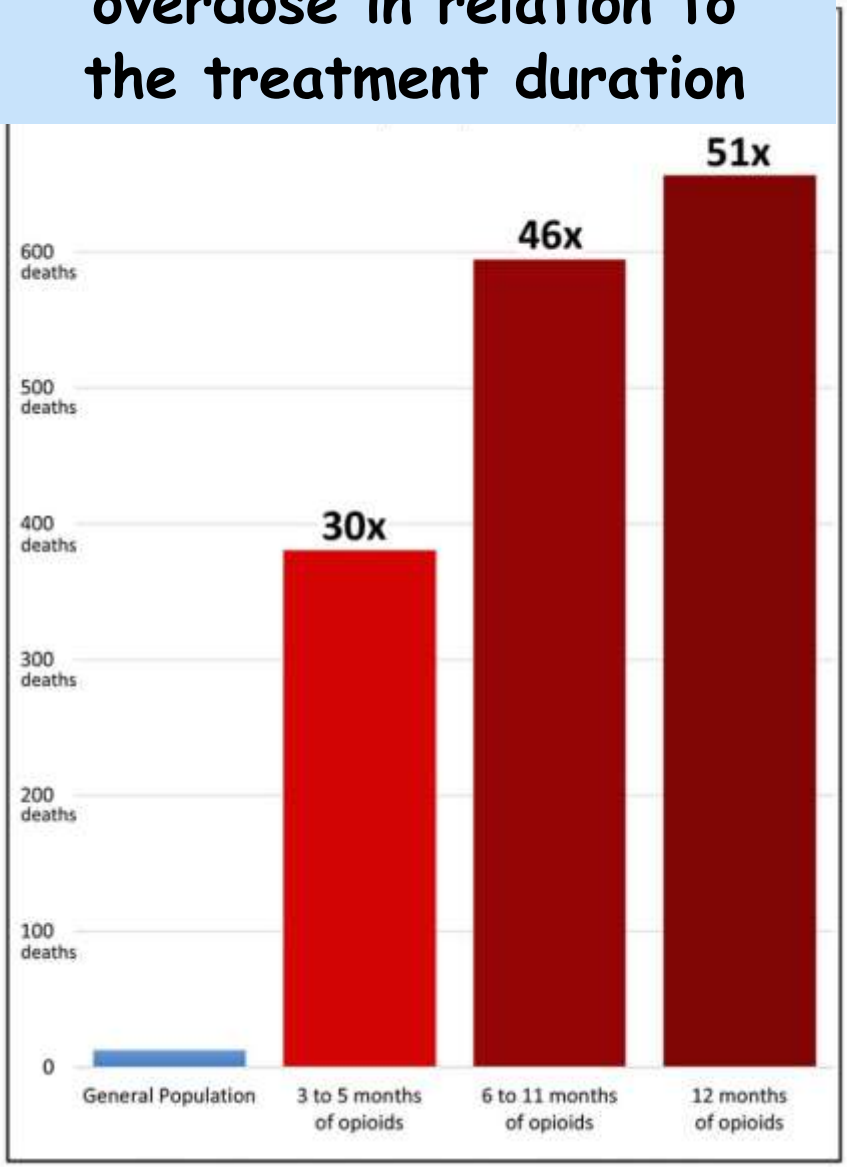


Sleep disordered breathing and chronic respiratory failure in patients with chronic pain on long-term opioid therapy



Rose AR. *J Clin Sleep Med* 2014

Risk of death from opioid overdose in relation to the treatment duration



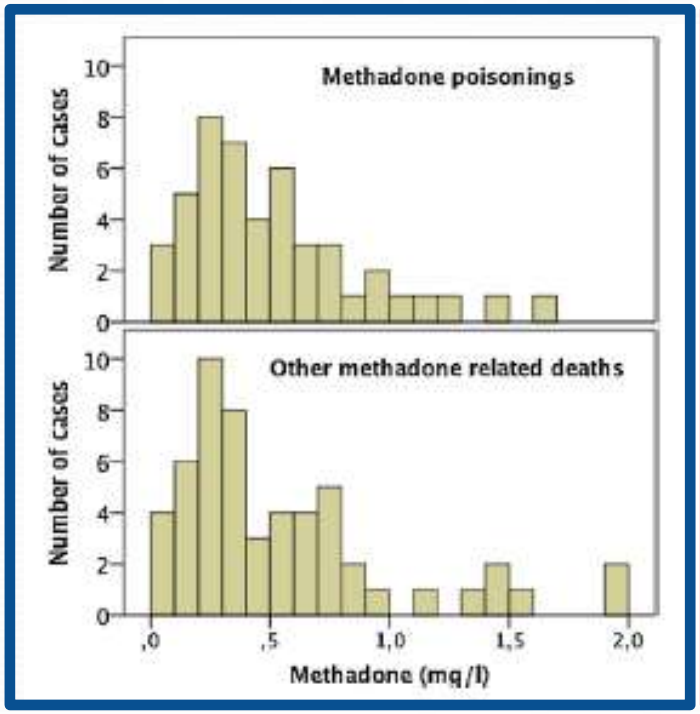
AGO graph from Massachusetts Department of Public Health data

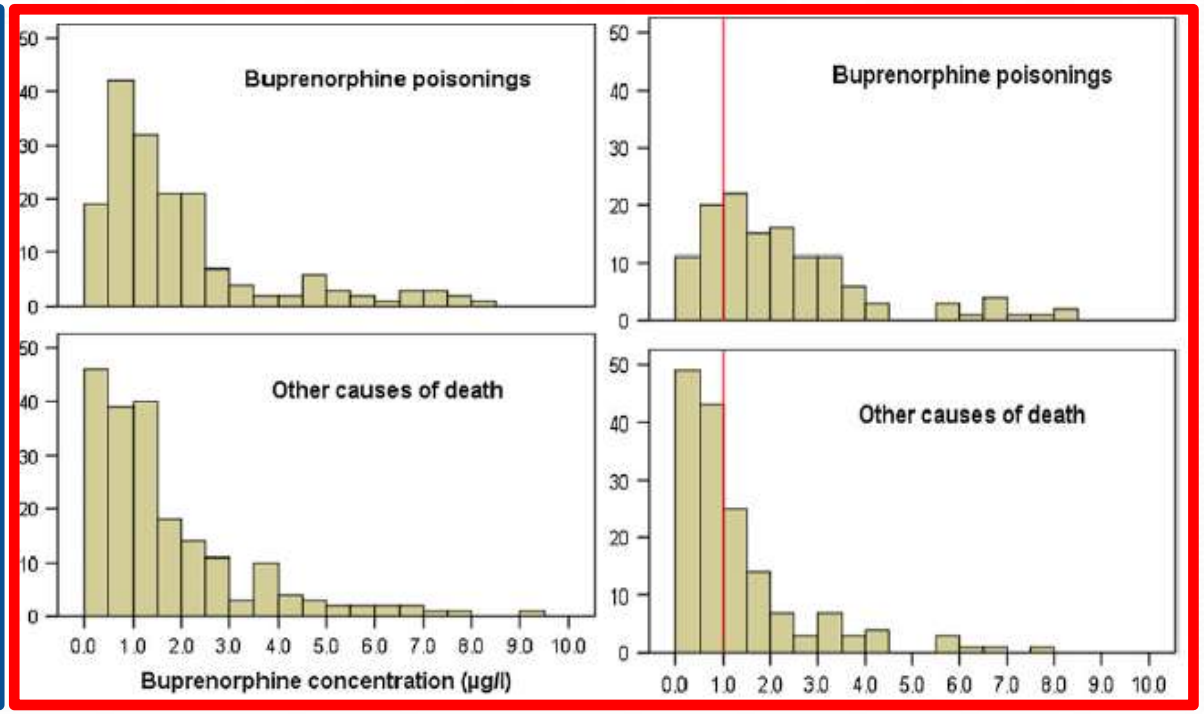
Risk factors for severe respiratory depression from prescription opioid overdose

Prescription opioid	*SRD rate (%)*	*RR (descending)*	*95% CI*
Tapentadol	2/2 (100)	27.0	3.9–185
Fentanyl	5/6 (83.3)	22.5	3.2–159
Oxymorphone	2/3 (66.7)	18.0	2.2–144
Methadone	59/116 (50.9)	13.7	2.0–95
Hydromorphone	4/9 (44.4)	12.0	1.5–94
Morphine	5/12 (41.7)	11.3	1.5–86
Oxycodone	40/124 (32.3)	8.7	1.3–60
Hydrocodone	9/31 (29.0)	7.8	1.0–58
Buprenorphine	2/7 (28.6)	7.7	0.8–73
Tramadol	3/12 (25.0)	6.8	0.8–58
Codeine	1/27 (3.7)	1.0 (ref)	–

Fox LM. *Addiction* 2018

Opioid-attributed death: role of the dose?





Methadone-related deaths

Buprenorphine-related deaths

Häkkinen M. *Forensic Sci Int* 2012

Häkkinen M. *Eur J Clin Pharmacol* 2011

Could chest wall rigidity be a factor in the rapid death from illicit fentanyl abuse?

(N= 48)

Acute chest wall rigidity is a well-recognized complication

1- Deaths occurred with fentanyl in the therapeutic range (1–2 ng/ml) in apparent non-naive opiate abusers

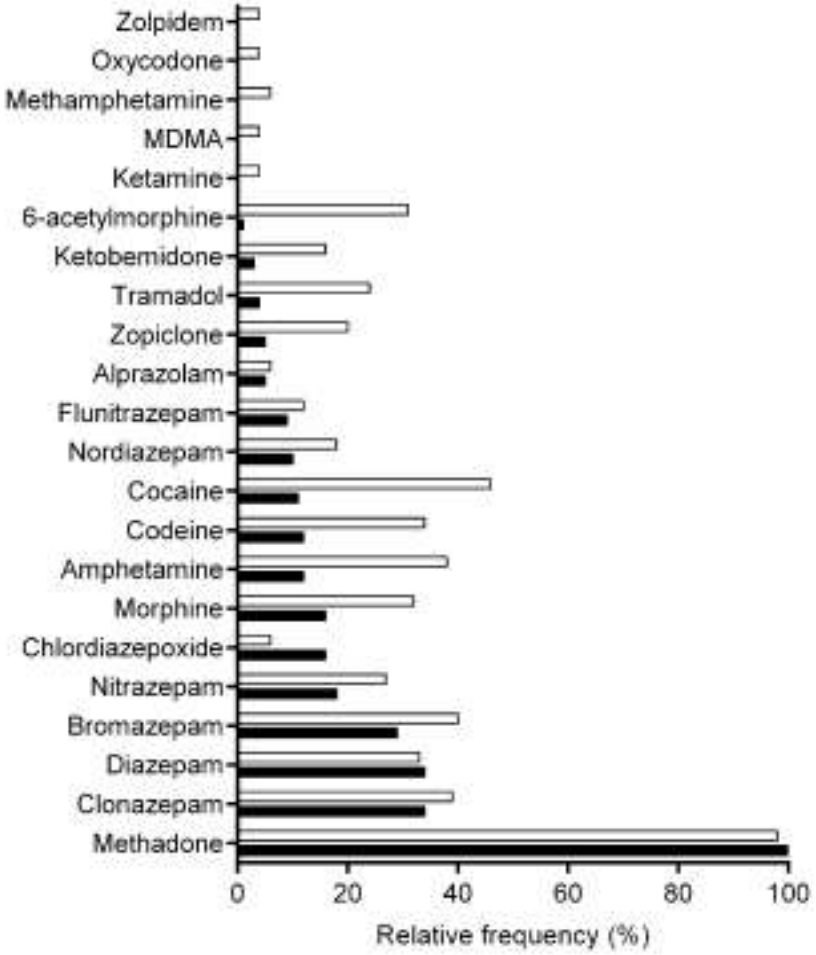
questioning the onset of dose-dependent respiratory arrest as mechanism of death

2- Lack of measurable norfentanyl in half of the cases despite high fentanyl
- No correlation between elevated fentanyl and rises in norfentanyl

suggesting a very rapid death, consistent with acute chest rigidity

Burns G. *Clin Tox* 2016

Drug-drug interactions



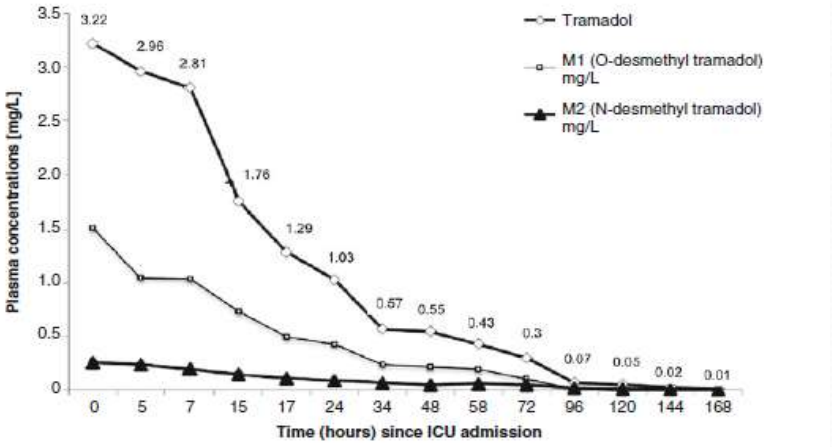
Abundance of hypnotics and drugs of abuse in blood (black) and proximal hair segments (white) in 99 methadone-related fatalities.

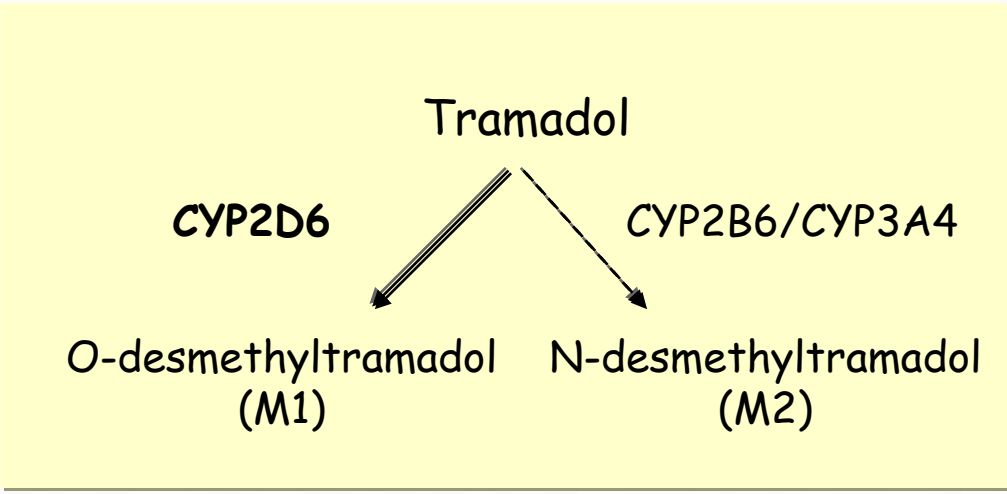
Based on segmental hair analysis, continuous exposure of methadone suggested that reduced tolerance of methadone is not a critical factor among methadone-related fatalities.

In contrast, a high abundance of co-ingested CNS depressants suggested that adverse effects from drug-drug interactions are more important risk factors for fatal outcome

Nielsen MK. *Forensic Sci Int* 2015

Vulnerability related to gene polymorphism: Near-fatal tramadol cardiotoxicity in a CYP2D6 ultrarapid metabolizer





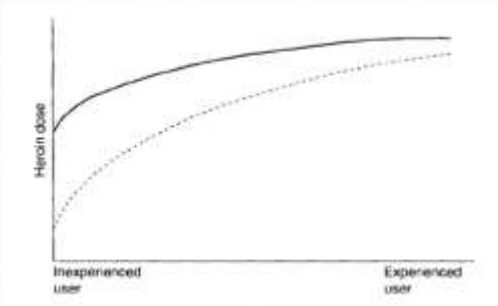
- Ultrarapid metabolizer phenotype suggested by tramadol/M1 metabolic ratio
- Heterozygous for duplicated wt allele predictive of CYP2D6 ultrarapid metabolizer phenotype

+ Ketoconazole at inhibitory concentration of CYP3A/CYPB6 (200 ng/ml)

Elkalioubie A. *Eur J Clin Pharmacol* 2011

The role of tolerance and abstinence

Tolerance theory



Tolerance

↓

Dose increase

↓

Death

White JM. *Addiction* 1999

Abstinence theory

Abstinence

↓

Tolerance decrease

↓

Re-consumption

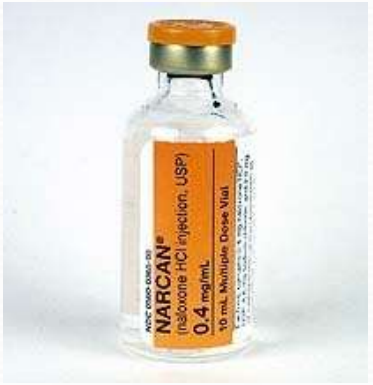
↓

Death

Druid H. *Forensic Sci Int* 2007

Naloxone: pharmacology properties

- Pure opioid antagonist at mu (high affinity), kappa, and delta receptors
- No agonist properties
- High first-pass metabolism (poor oral bioavialability)
- Short-plasma half-life 50 min
- Duration of action: 1-4 h
- Administered IV, IM, SC, IN



Widely used to reverse opioid toxicity

Dose-dependent reversal of opioid agonist effects

High dose may precipitate acute opioid withdrawal syndrome

Comparison of heroin, methadone and BUP overdoses

	Heroin (N = 26)	Buprenorphine (N = 39)	Methadone (N = 19)	*p*
Suicide	12%	18%	58%	**0.0007**
Co-ingestions	73%	95%	89%	**0.04**
Glasgow Coma Score	5 [3 - 9]	7 [4 - 10]	4 [3 - 10]	0.1
Respiratory rate	10 [6 - 13]	12 [8 - 15]	10 [6 - 13]	0.4
SpO_2 (%)	82 [64 - 95]	94 [87 - 98]	91 [82 - 97]	**0.05**
pH	7.29 [7.17-7.34]	7.35 [7.24-7.38]	7.33 [7.23-7.42]	0.07
$PaCO_2$ (mmHg)	51 [45 - 55]	50 [45 - 66]	50 [36 - 57]	0.7
Mechanical ventilation	46%	41%	47%	0.6
Response to naloxone	81%	0%	71%	**<0.0001**
Response to flumazenil	0%	87%	60%	**0.02**

Mégarbane B. *JSAT* 2010

Preventing opioid overdose deaths With take-home naloxone

- Death from opioid overdose occurs frequently at home, 1-3 h after exposure and often in the presence of bystanders (80%)
- BCLS by bystanders are generally not sufficient

Number of programs of naloxone distribution	Number of naloxone vials distributed over one year	Number of program participants	Number of reported opioid overdose reversals
136	140 053	152 283	26 463

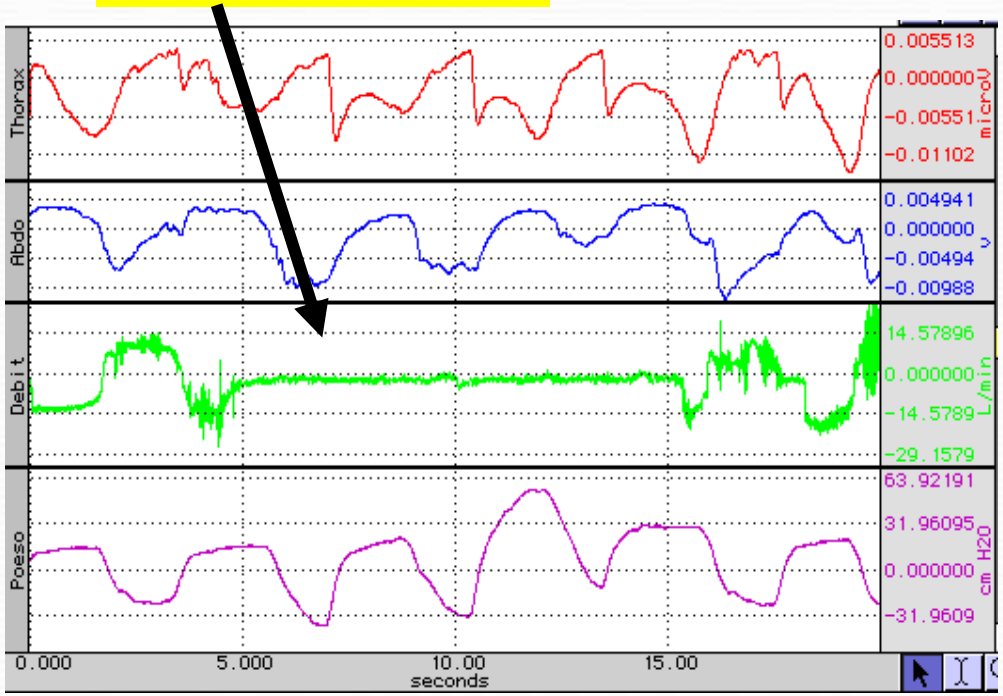
Wheeler E. *MMWR Morb Mortal Wkly Rep* 2015

3

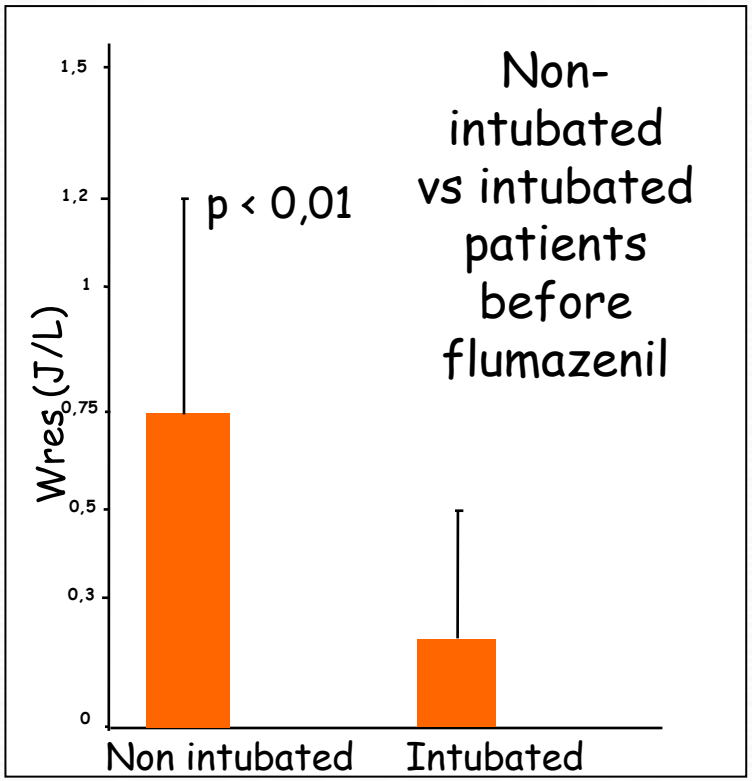
Peripheral respiratory depression

Mechanisms of respiratory insufficiency in coma involving benzodiazepines

Obstructive apnea



Non-intubated patient before flumazenil

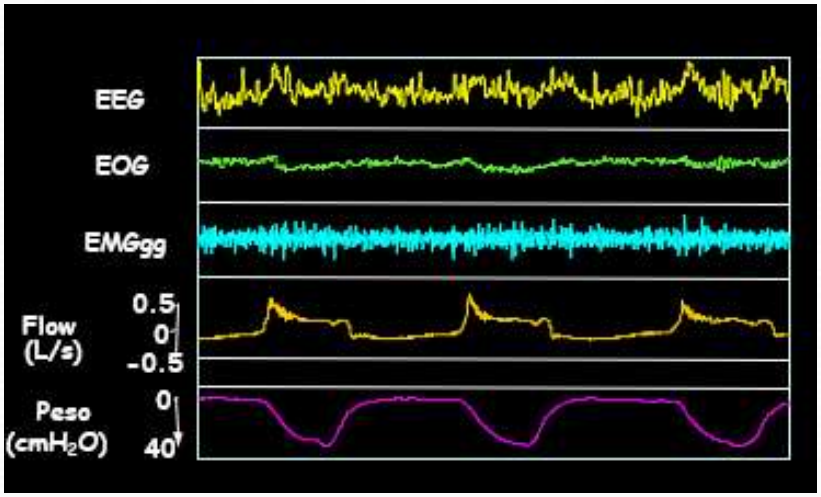


Gueye P. J Toxicol Clin Toxicol 2002

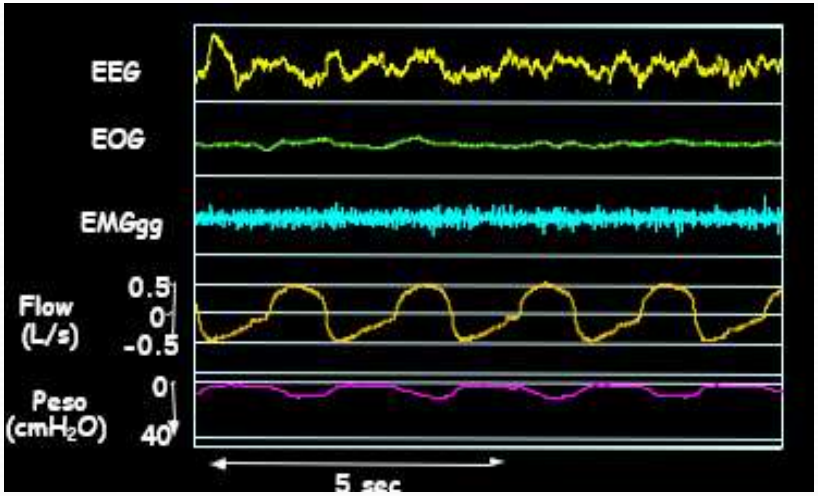
Increase in the resistive load and respiratory work

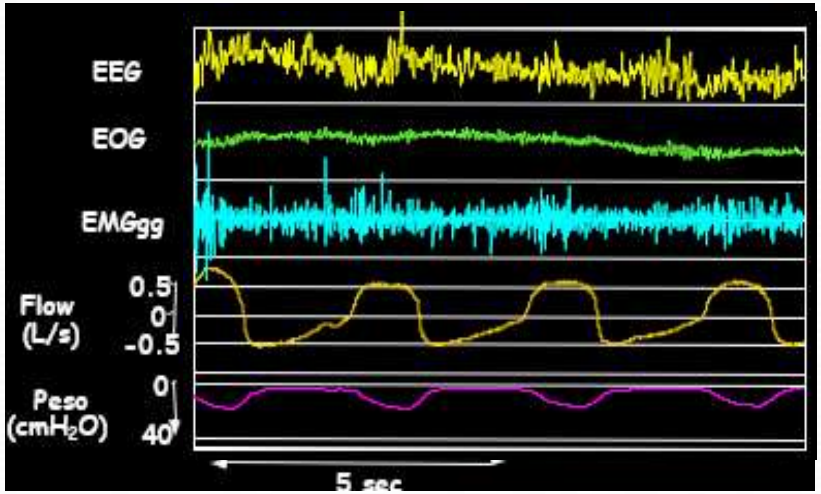
Obstructive mechanism of respiratory insufficiency in benzodiazepine-induced coma

Tracheal intubation



Flumazenil injection





Gueye P. J Toxicol Clin Toxicol 2002

BUP / BZD interaction

Hypothesis: PD interaction with addition of different physiological effects

Mégarbane B. *Forensic Int Sci* 2011

Benzodiazepines :

- Alteration of Upper Airways Dilators (GABA $_A$)

  ➔ hypopnea, obstructive apnea

- Diaphragmatic dysfunction

Increase of the workload of breathing

Opioids

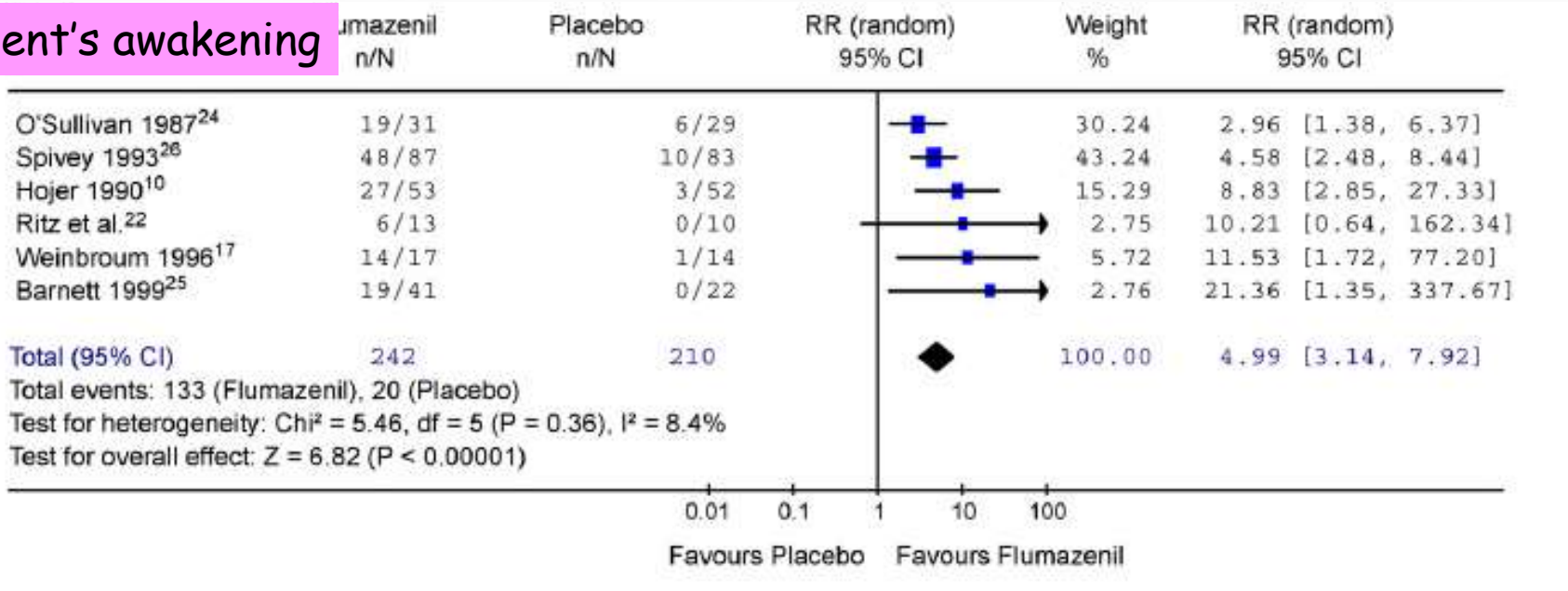
- Decrease of the ventilatory response to
  - Inspiratory load
  - Hypoxia
  - Hypercapnia

Depression of the ventilation centres

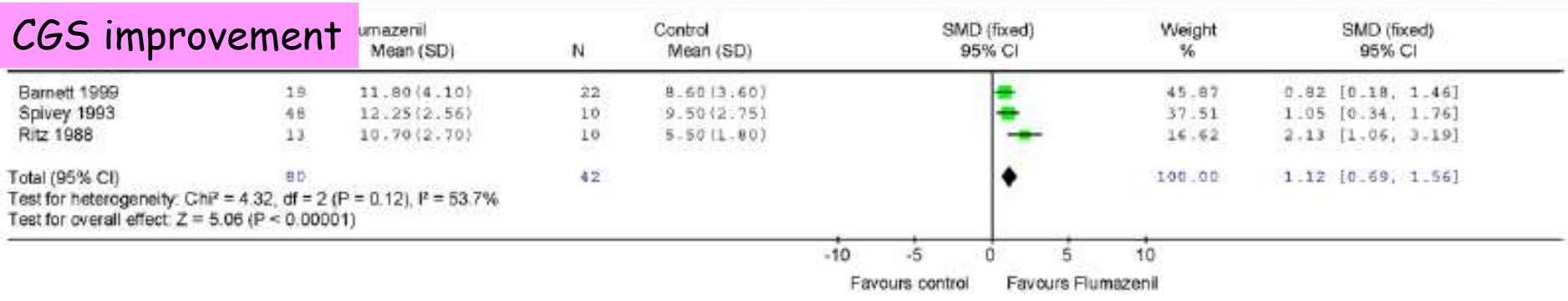
The combination of effects may result in respiratory depression and death

Should we use flumazenil in presumed toxic coma? (1)

Patient's awakening



CGS improvement



Ngo AS. *Resuscitation* 2007

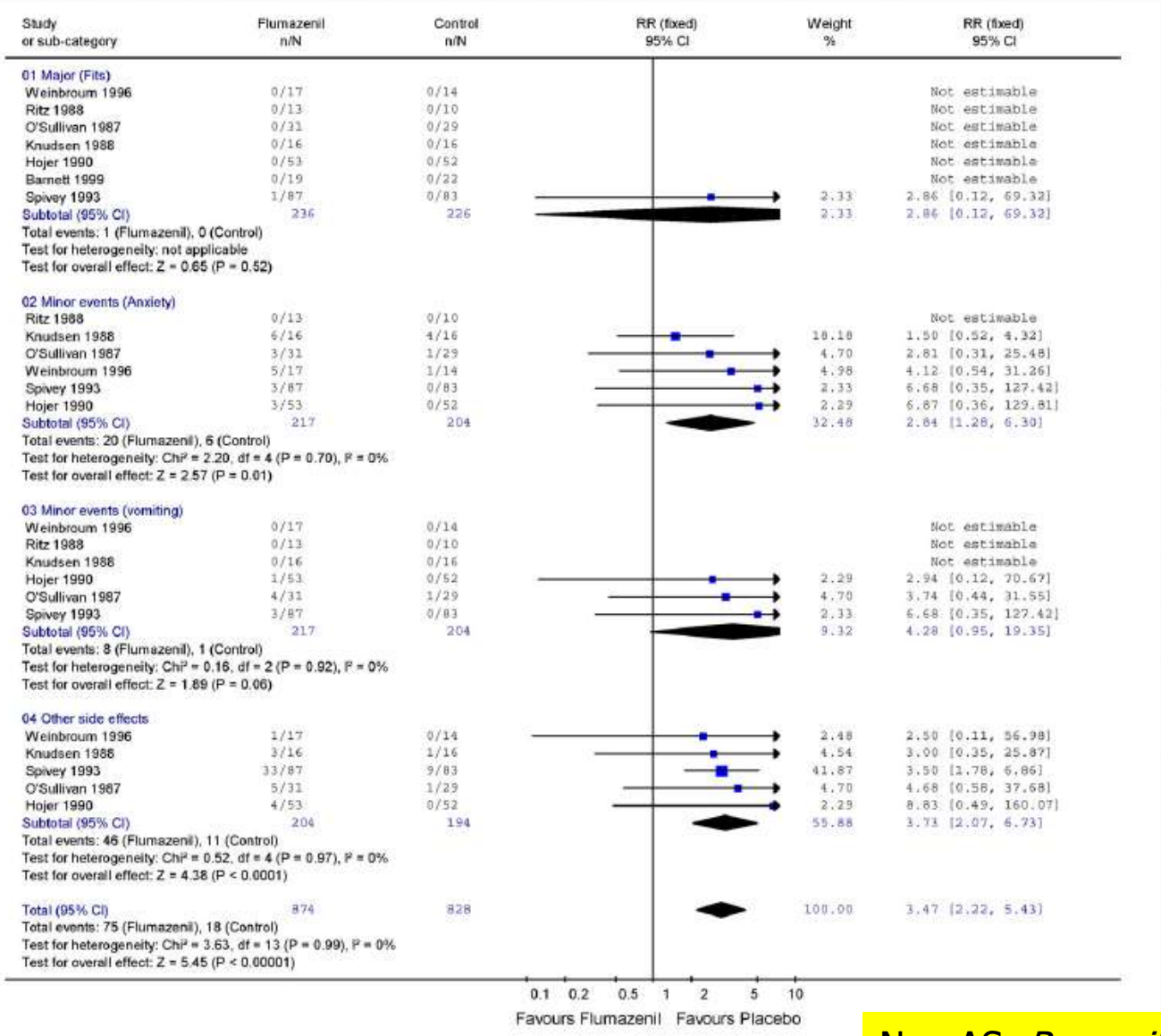
Should we use flumazenil in presumed toxic coma? (2)

Major ADR

Anxiety

Vomisiting

Minor ADR



Ngo AS. *Resuscitation* 2007

Flumazenil does not increase the global costs of patient management in the ICU

Factor	Flumazenil	Placebo	*p* Value
Number	19	22	
Emergency room	244 ± 106	276 ± 111	NS
Nursing	140 ± 59	151 ± 51	NS
ER physician fee	93 ± 29	98 ± 33	NS
Drug	101 ± 57	5 ± 2	<.001
Inpatient	402 ± 1920	1258 ± 1100	NS
Medical consult	148 ± 77	109 ± 27	NS
ICU consult	400 ± 71	276 ± 63	NS
ICU	327 ± 2410	1245 ± 490	[b]
Total cost	1524 ± 2520	1432 ± 1420	NS

[a]Canadian dollar = 0.73 United States dollar; [b]sample size inadequate to compare costs.

Barnett R. *Crit Care Med* 1999

Guidelines for routine flumazenil use

- 0.1 to 0.3 mg IV bolus
- Titration to avoid withdrawal syndrome
- More elevated dosage regimen if multi-drug poisoning: up to 2 mg bolus
- Efficient in poisonings with assimilated molecules (zopicolone and zolpidem)
- Caution if tricyclic antidepressants or carbamazepine co-ingestion
- Add bolus or continuous infusion (0.3-0.5 mg/h) to maintain consciousness
- Significant improvement in respiratory conditions to avoid tracheal intubation

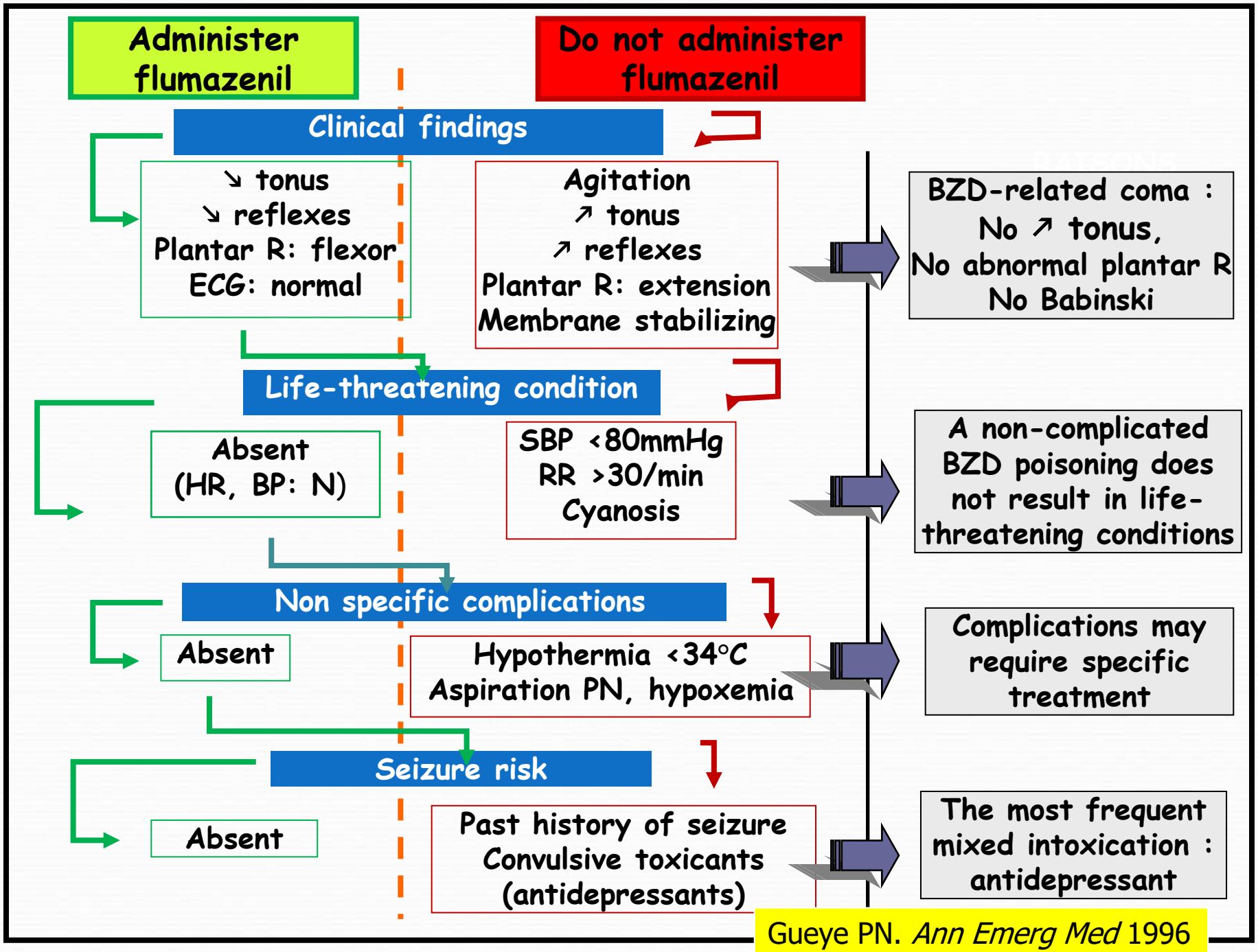
- Debated utilization in ethanol poisoning or liver encephalopathy
- Efficient and safe utilization in elderly, children, babies, pregnant women

Weinbroum AA. *Drug Safety* 1997

Flumazenil in children:

- 10-20 µg/kg IV bolus
- Experience (N=83; 2 years [3 months,12 yrs]): excellent tolerance, no convulsion

Kreshak AA. *Pediatr Emerg Care* 2012


Administer flumazenil
Do not administer flumazenil
Clinical findings
↘ tonus
↘ reflexes
Plantar R: flexor
ECG: normal
Agitation
↗ tonus
↗ reflexes
Plantar R: extension
Membrane stabilizing
BZD-related coma :
No ↗ tonus,
No abnormal plantar R
No Babinski
Life-threatening condition
Absent
(HR, BP: N)
SBP <80mmHg
RR >30/min
Cyanosis
A non-complicated BZD poisoning does not result in life-threatening conditions
Non specific complications
Absent
Hypothermia <34°C
Aspiration PN, hypoxemia
Complications may require specific treatment
Seizure risk
Absent
Past history of seizure
Convulsive toxicants
(antidepressants)
The most frequent mixed intoxication : antidepressant
Gueye PN. Ann Emerg Med 1996

4

The GHB threat

Recreational GHB/GBL use and overwhelming issue of drug-facilitated sexual assaults

- GHB: colorless and odorless slightly salty/bitter lliquid
- GBL: colorless oily water-soluble liquid
- **Dosage:** 2-5 g /dose with 1-3h interdoses, difficult calibration


M Santé

La consommation récréative de GHB alarme la nuit parisienne

Longtemps surnommé « drogue du violeur », le GHB est aujourd'hui souvent consommé de façon volontaire et récréative, comme son cousin le GBL. Mais les risques sont méconnus et les accidents se multiplient.


Préoccupante mode du GBL, une drogue proche du GHB, dans les clubs parisiens

Par AFP — 17 avril 2018 à 13:56


Un jeune homme meurt d'une overdose de GBL

Un drame qui met en lumière le grand retour, dans le milieu de la nuit, de ce produit particulièrement dangereux. Enquête.


Le Parisien

ALERTE AU GHB

ENQUÊTE La « drogue du violeur » est de plus en plus utilisée comme un stupéfiant classique. Cette banalisation affole les organisateurs de soirées et les autorités.

Toxicity attributed to GHB

- Dose- and concentration-effect relationships

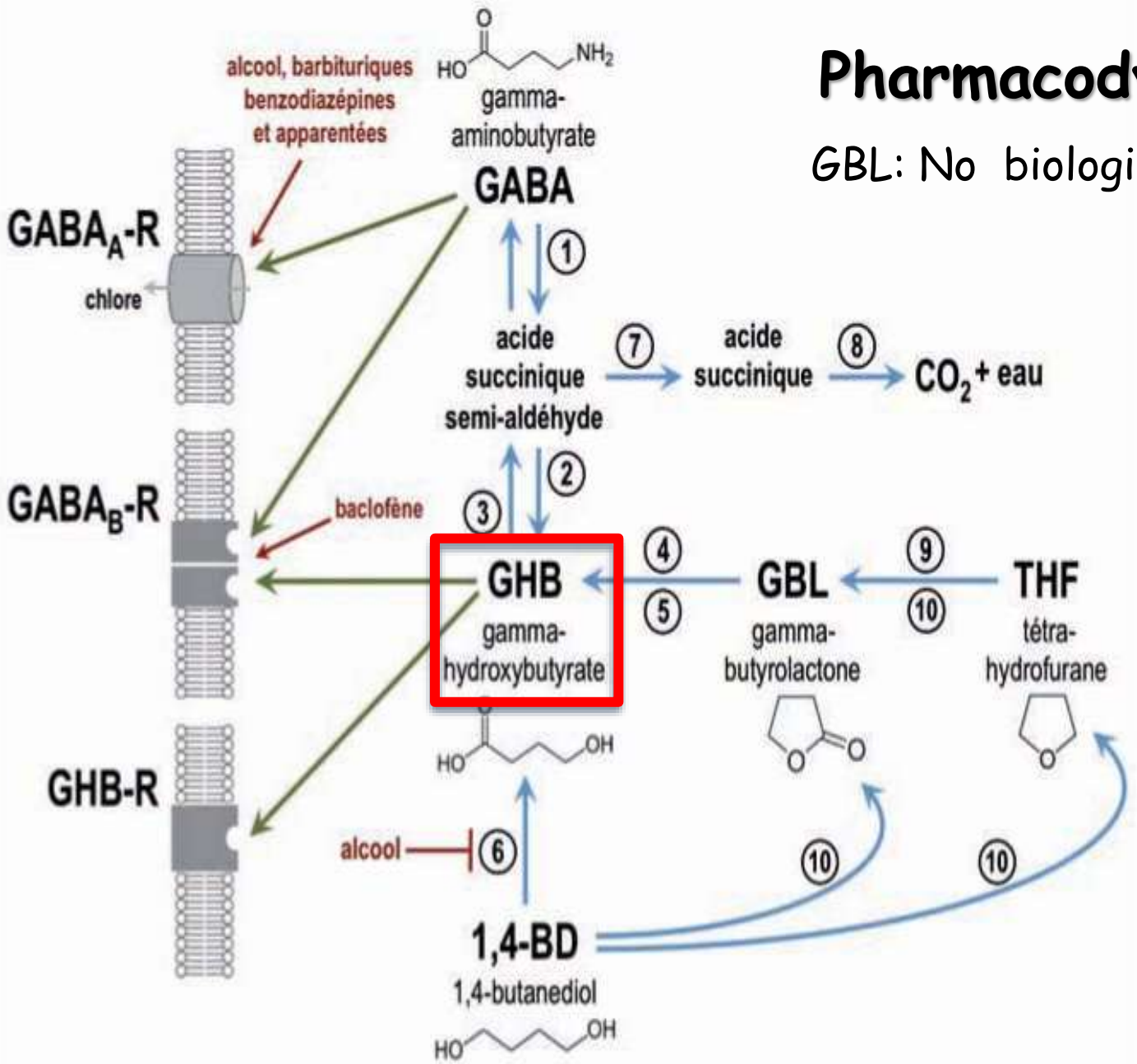
Dose (mg/Kg)	Symptoms
10	Amnesia, myorelaxation, hypotonic, dizziness, myoclonus
20 - 30	Euphoria followed by sleepiness
30 - 50	Sedation, nausea/vomitig
50 - 100	Non-reactive coma (G-hole), respiratory depression, seizures, bradycardia, hypotension, nystagmus, myosis/mydriasis

- Tight therapeutic index
- Inter-individual variability
- Tolerance development if repeated use
- Aspiration, ↘K+, ↗ WBC, ↗CK, AVB
- Withdrawal: 1-6h, peak 24h, duration 14d

Shep LJ. *Clin Tox* 2012

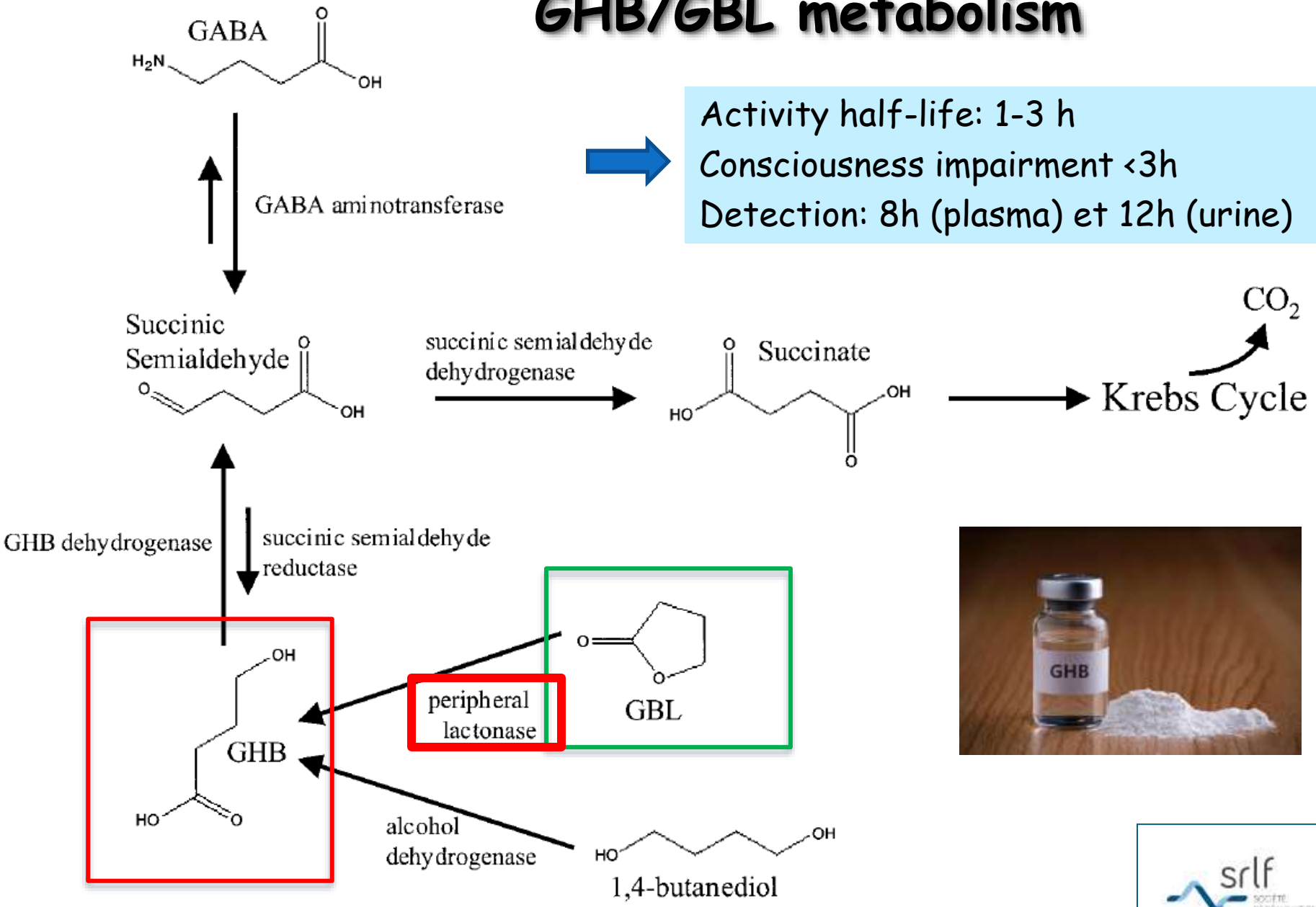
Pharmacodynamics

GBL: No biological activity



Endogenous GHB (blood < 5 µg/mL and urine < 10 µg/mL)

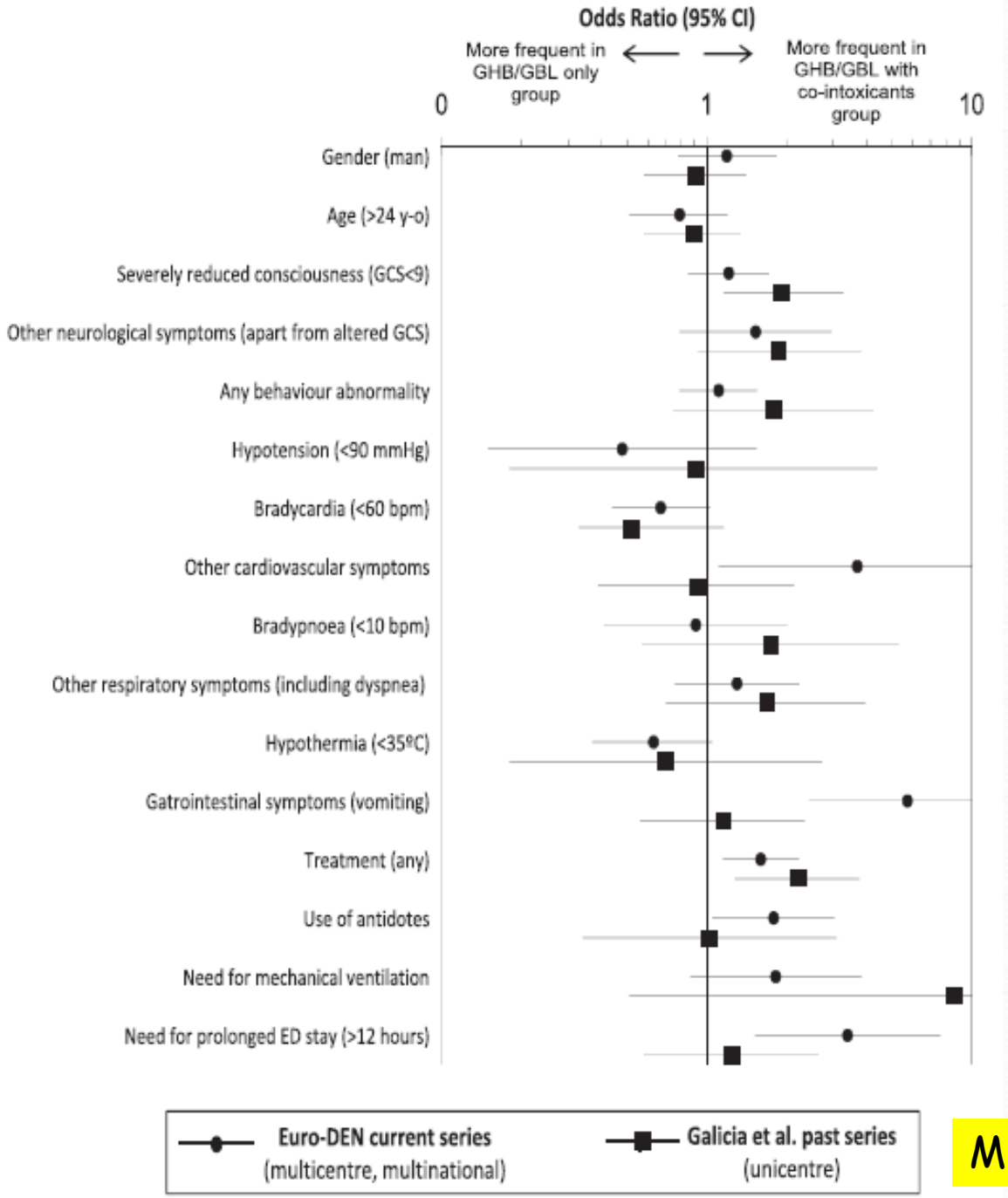
GHB/GBL metabolism



Activity half-life: 1-3 h

Consciousness impairment <3h

Detection: 8h (plasma) et 12h (urine)



Mixed GHB/GBL poisonings

Miro O. *Tox Lett* 2017

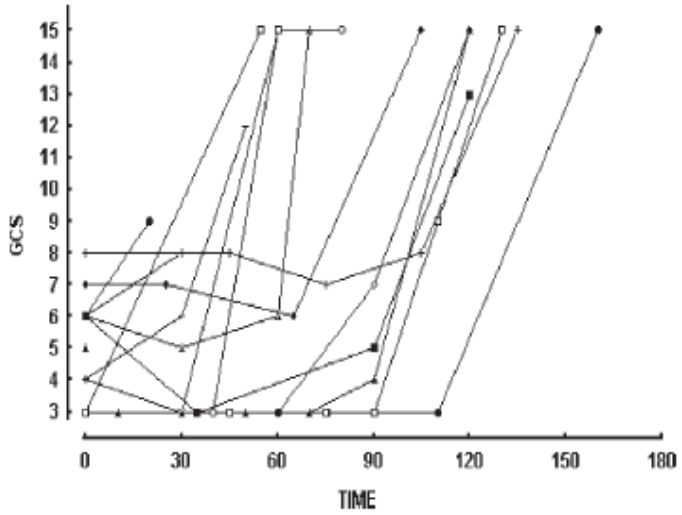
Rapidity of awakening in GHB poisoning

21 participants to 6 rave parties admitted with GCS ≤8

15/21: positive GHB screening

Plasma [GHB] : 212 µg/ml (112 - 430)

14/15: multi-drug ingestions



GCS ≤8 during 90 min (30 - 105)

GCS change from ≤8 to ≥12: 30 min (10 - !

Patient subgroup with GCS =3:

Remained at GCS 3 during 60 min (30 - 110)

GCS change from 3 to 15 in 30 min (20 - 60)

No patient was further intubated

Van Sassenbroek D. *Clin Tox* 2007

Take home messages

- **Aspiration pneumonia** is common in the comatose patient. Risk factors include **impairment of swallowing & alteration in consciousness**. Aspiration pneumonia is associated with **severity**, prolonged ICU stay, and **increased mortality**.
- **Drug-induced respiratory depression** is frequent. CNS depression attributed to **opioid and GHB** represents a growing concern. **Diagnosis** at the bedside is based on respiratory rate, SpO_2 and blood gas. Management is supportive.
- In patients with GCS <8, **tracheal intubation** should not be systematic. Decision should take into account the drug properties and its PK as well as the level of encephalopathy and respiratory/circulatory findings.
- **Antidotes** (naloxone and flumazenil, according to the toxidrom) can avoid intubation in selected patients. Their use is safe if respecting contra-indications.
- Adjunctive role of the **physiotherapist** to prevent and treat complications resulting from drug-related neuro-respiratory effects