

# Acute Pain Management in the Opioid Tolerant Patient

Jean-Louis Horn, MD

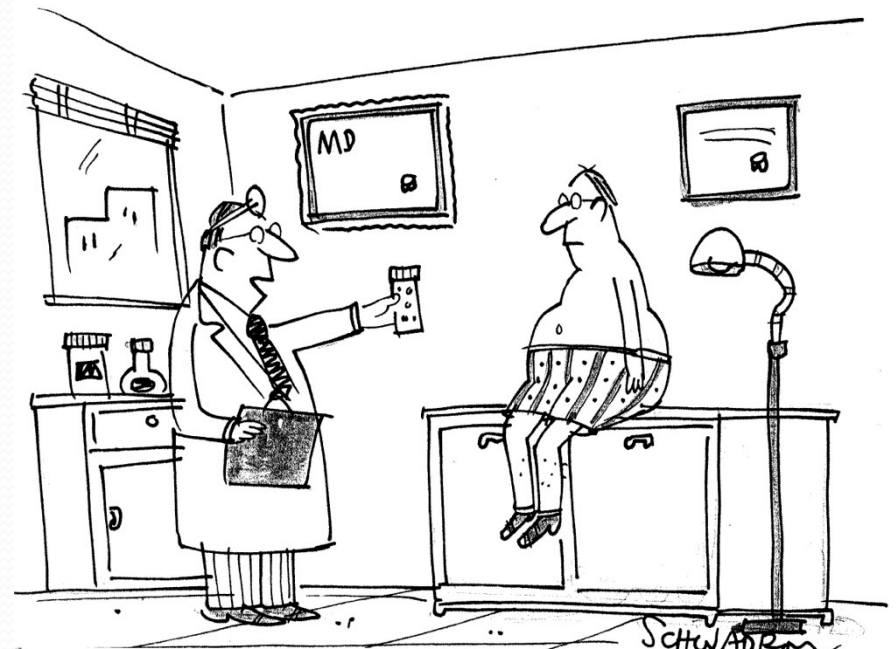
Professor, Chief, Division of Regional Anesthesia

Department of Anesthesiology, Perioperative and Pain Medicine



# Disclosure

- Consultant for Teleflex Medical
- Consultant for Halyard Health
- Consultant for Edan Medical
- Research support from Zyno Medical



"Under disclosure rules, I'm required to tell you I own stock in the company whose drug I'm prescribing."



# Overview

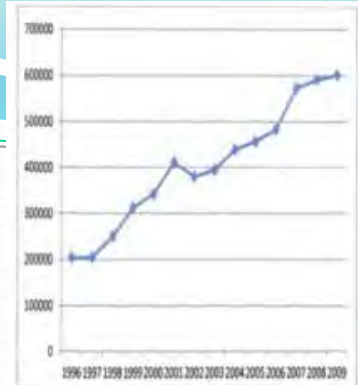
- *Definition and Scope*
- Management modalities
- Conclusions



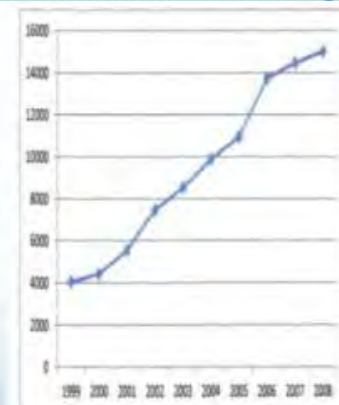
# Post-Operative Pain

- **Pain response a to nociceptive stimulus is subjective and highly variable**
  - Influenced by psycho-social factors (anxiety, gender, cultural...)
  - Genetic factors
  - Previous pain experience/current pain level
  - Previous exposure to opioids

# Opioid Epidemic



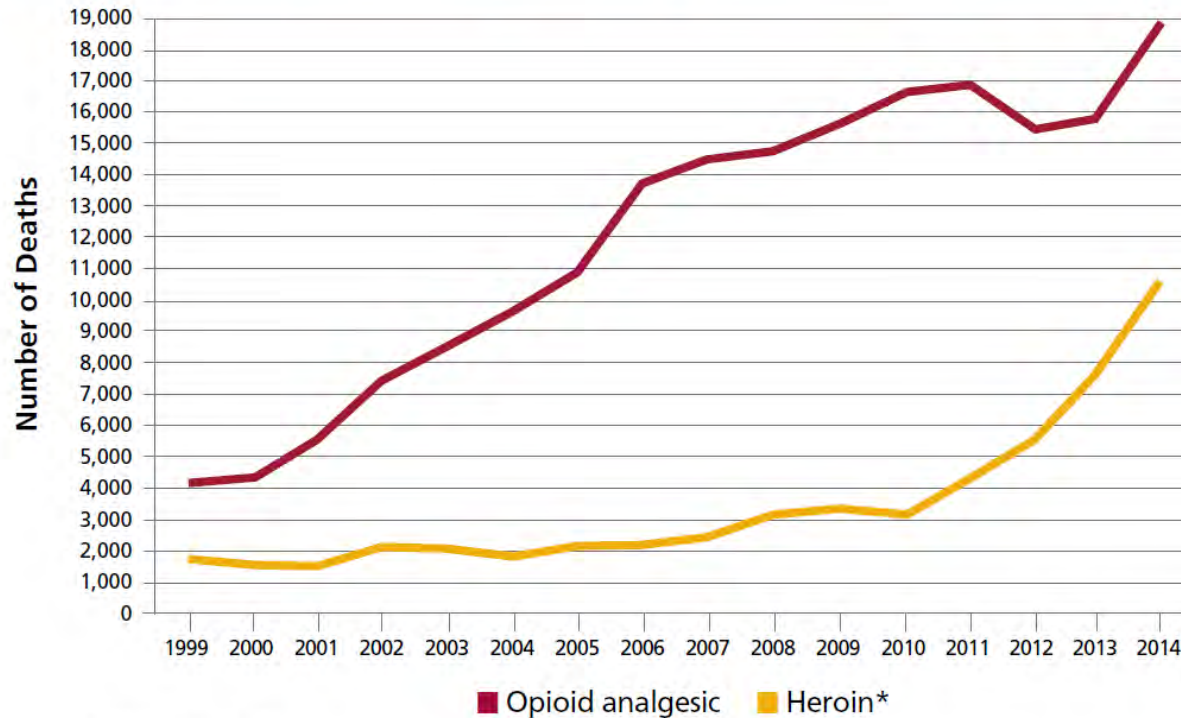
DEA Production Quotas for Schedule II Opioids, 1996-2009 (kg). Includes quotas for codeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oryxmorphone and thebaine. Source: DEA website.



Annual deaths from opioid analgesics, United States, 1999-2008. Source: CDC.

US Production Quotas Vs. Overdose Deaths

## U.S. Deaths from Opioids & Heroin: 1999-2014



\*Heroin includes opium.

1999-2013 Statistics: CDC/NCHS NVSS Multiple Cause of Death Files.

2014 Statistics: American Society of Addiction Medicine (ASAM), Opioid Addiction: 2016 Facts & Figures.

# Opioid Tolerance

*A phenomenon where the pain relieving effects of the medication decrease over time, so the patient feels they need more of the drug to achieve the same effect.*



**WITHDRAWAL  
SYMPTOMS  
CRAVING  
OPIOID SEEKING**



**TOLERANCE**



**DEPENDENCE**



# FDA Definition of Opioid tolerance

More than 60 mg of oral morphine equivalence  
(MEQ) for a least 7 days

## Mechanism

Presynaptic EAA release by opioids  
Postsynaptic NMDA activation  
Down regulation and desensitization of receptors

Pain Management Nursing. 2007;8(3):113-21

# Opioid Induced Tolerance

- Can develop after a short/acute exposure, not just after long term usage
- High potency opioid may be more “potent” to induce tolerance
- But **no** tolerance to miosis and constipation!!!
- Chronic opioid users require 3-4x dosage of opioid to control their pain postoperatively

Pain 1995;61:195-201

Anesth Analg 1993;76:302-7



# Opioid Induced Hyperalgesia

- State of nociceptive sensitization caused by exposure to opioids
- Paradoxical response to opioids where exposure to treat pain increase sensitivity to certain painful stimuli
- Result in loss of efficacy of opioids

Pain Physician. 2011; 14:145-61

# Overview

- Definition and Scope
- *Management modalities*
- Conclusions



# Basic Principles

- Identify the specific problem
  - Pain and related affect (psycho-social situation)
  - Current opioid usage and dosage
  - Current adjunct therapy
- Plan
  - Manage/stabilize psycho social issues
  - Maximize systemic non-opioid adjuvants
  - Plan for Regional and Local anesthesia
  - Manage and plan perioperative opioid therapy

# Psycho-Social issues

- Preoperative counseling and setting up reasonable expectations ~ placebo effect
- Refer to pain clinic to ensure multidisciplinary care when the situation is out of control
- **Not a time to treat dependence**
- Opioid-phobia should not lead to poor planning
- Keep the baseline opioid and supplement as needed
- **Postop dosage is difficult to predict**



# Adjuvant Therapy

- NSAIDS
- COX-2 inhibitors
- Acetaminophen
- Neuropathic pain medication
- Vit C
- Mg<sup>++</sup>
- Ketamine
- Regional/Local anesthesia
- “Methadone”
- “Neuromodulation”

# Ketamine

- Prevent/reverse central sensitization to opioids
- Small dose (0.25mg/kg) added to morphine (0.1mg/kg) postop decrease VAS from 6/10 to 1.47/10 compare to 3.8/10 with morphine alone while maintaining better oxygenation, less N/V
- Intraoperative use in opioid tolerant patients, the effect was still present 6 weeks after surgery (pain, opioids and side effects)
- Seems more efficacious when given before opioids
  - Anesth Analg 2003 (93) 789-95
  - Anesthesiology 2010 (113) 639-46

# Ketamine Side Effects and Myths

- Tachycardia and hypertension
  - Easy to avoid with low dose and slow titration
- Hallucinations
  - Minimize the impact with proper education
  - Mostly enjoyed by our patients ~ trip
- Cognitive dysfunction in the elderly
  - Unfounded and in fact the opposite most likely due to the opioid sparing effect
- Delay emergence from anesthesia
  - Unfounded and in fact may be the opposite

# Local and Regional Anesthesia

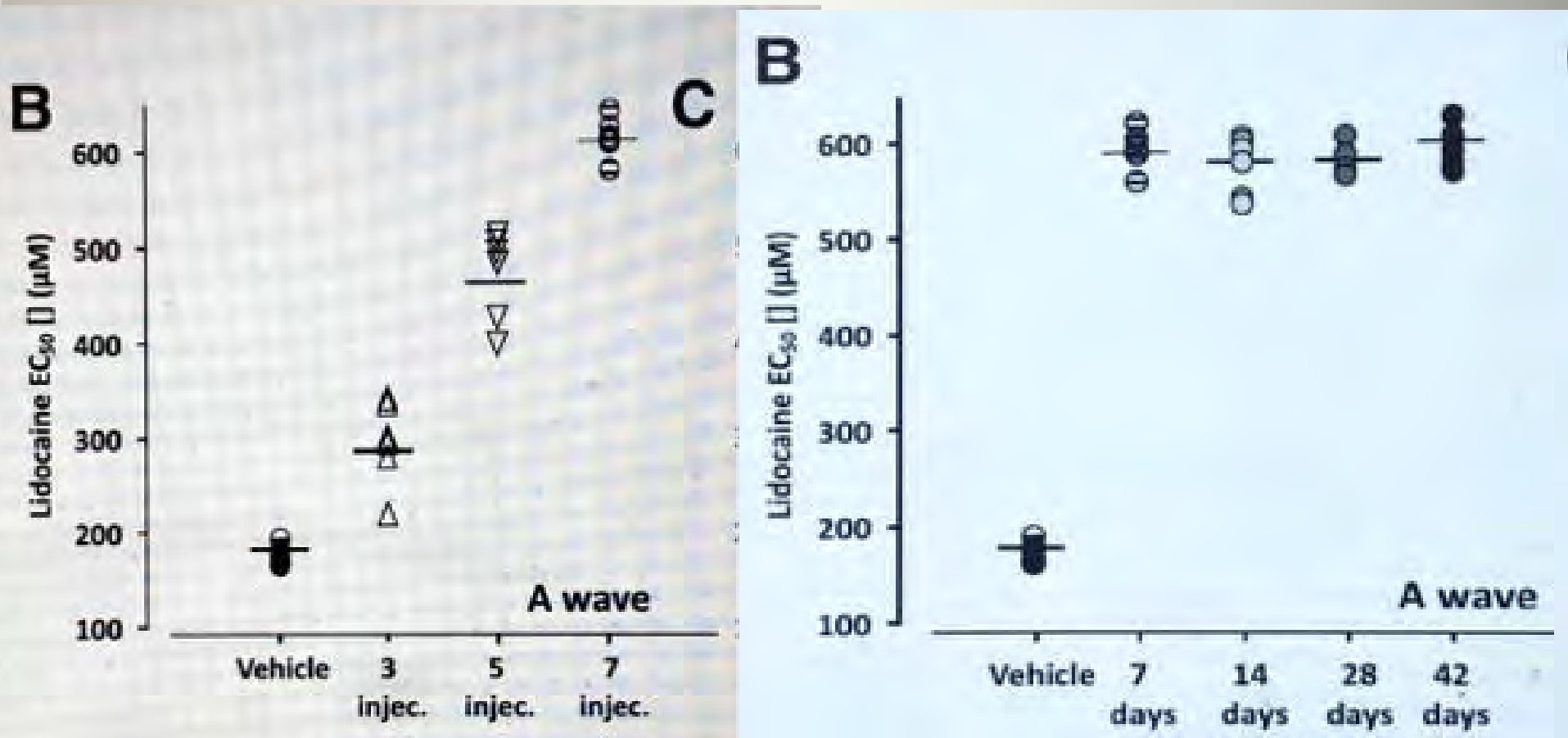
- Spinal for intraop anesthesia
- LIA
- Peripheral Nerve Block (catheter based):
  - AC vs Fem (+ sciatic) for TKA
  - LPB for THA
- “Epidural”
- Opioid tolerance induced local anesthetics tolerance



# Opioid-induced Loss of Local Anesthetic Potency in the Rat Sciatic Nerve

Qing Liu, M.D., Ph.D., Michael S. Gold, Ph.D.

Anesthesiology: Oct 2016



# Opioid Management

- Keep the baseline opioid (not a good time for weaning opioids)
- Supplement as needed, keeping in mind that the patient may require higher dosage
- And is at increase risk of serious complication related to opioids including overdosing

# WHO Pain Management Ladder

## WHO Cancer Pain Management Ladder

- Valid for **non-opioid** tolerant patient
- **Highlight the value of the non-opioids adjuvants**



# Methadone

- Long acting opioid with NMDA antagonist properties
- Prevent opioid induced hyperalgesia
- Relatively low rate of respiratory depression
- With ketamine, presents super additive NMDA antagonist action

J Pharmacol Exp Ther 1999. 289(2): 1048-53



# Conclusions

- CHALLENGE
- 9 FOLD increase of overdose
- Preop planing
  - Maintain current opioid baseline dose
  - Patient support/education
  - NSAIDS
  - COX-2 inhibitors
  - Acetaminophen
  - Vit C
  - Anti-epileptic (Gabapentin....)
- Intra-op
  - Ketamine
  - Regional/Local anesthesia
  - Alpha-2-agonists
- Postop
  - Continue multimodal pain management, (ketamine) + added opioids
- Future
  - Neuromodulation
  - Methadone



**Thank you**

