

## Opioid-Sparing Anesthesia: What Can We Learn from the Opioid Crisis?

Garry Brydges DNP, MBA, CRNA, ACNP-BC, FAAN  
2019 WVANA Spring Meeting

---

---

---

---

---

---

---

## Objectives

The learner will be able to:

- Describe the role of Opioid-Sparing Techniques in Anesthesia.
- Describe the outcomes achieved with opioid-sparing compared to traditional techniques.
- Differentiate the value of quality versus quantity of anesthesia through Opioid-Sparing Strategies

---

---

---

---

---

---

---

## Opioids: Public Health Issue

---

---

---

---

---

---

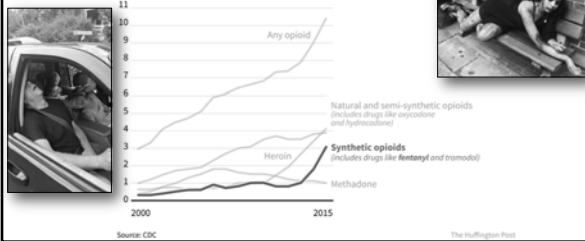
---



## Opioids: Public Health Issue

### Opioid-Related Deaths, Especially From Synthetic Opioids Like Fentanyl, Are On The Rise In The U.S.

Drug overdose deaths involving opioids, by type, per 100,000 population




---

---

---

---

---

---

---

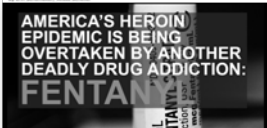
---

## Opioids: Public Health Issue

### Fentanyl Overdoses Are Rising And Science Can't Keep Up

Synthetic opioid formulas are evolving at a breakneck pace.

By Eric Lipton, Adam Scheraga



THE BLOG 06/06/2016 02:35 pm ET | Updated: Jun 06, 2016

### What Is Fentanyl? The Facts About the Opioid That Caused Prince's Death

By Health.com

---

---

---

---

---

---

---

---

## Opioids: Public Health Issue



3,000 X more potent than Morphine




---

---

---

---

---

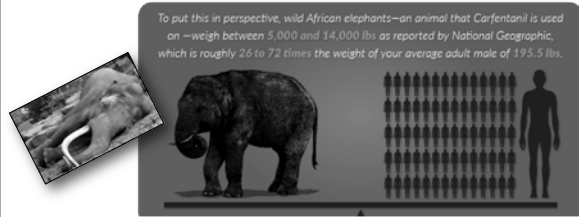
---

---

---



## Opioids: Public Health Issue



### 3 Marylanders die from carfentanil overdoses

WBALTV | Updated: 4:47 PM EDT Apr 24, 2017

---

---

---

---

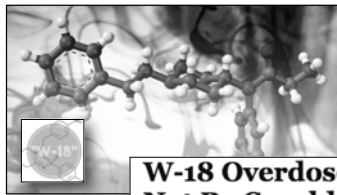
---

---

---

---

## Opioids: Public Health Issue



This new street drug is 10,000 times more potent than morphine, and now it's showing up in Canada and the U.S.

### W-18 Overdoses In Alberta May Not Be Curable With Naloxone Kits

The Huffington Post Alberta | By Sarah Rieger | Posted: 05/24/2016 5:53 pm EDT | Updated: 05/24/2016 5:59 pm EDT

---

---

---

---

---

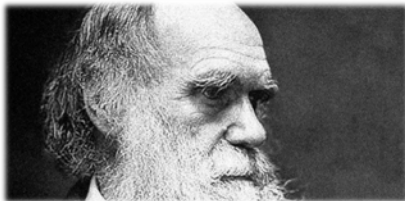
---

---

---

## Philosophically

Dr. Charles Darwin



Is this ... "Social" Natural Selection?

---

---

---

---

---

---

---

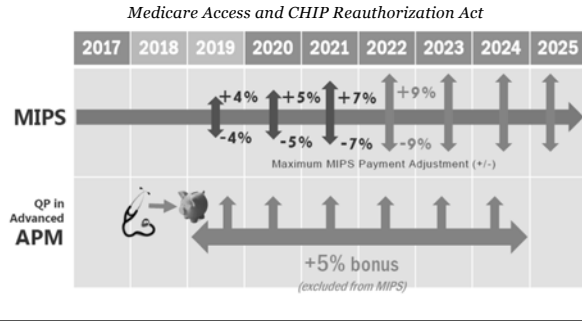
---







## Why is this Important? . . . Economists = MACRA




---

---

---

---

---

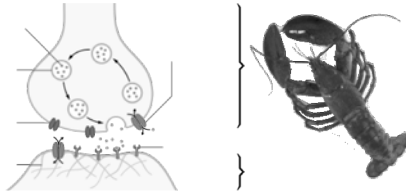
---

---

---

## Opioids: Public Health Issue

- How did we get here?
  - Imbalance Serotonin - Octopamine



Peterson, J. (2018) 12-Rules For Life: An Antidote to Chaos

---

---

---

---

---

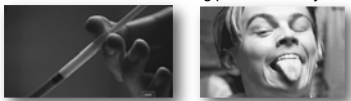
---

---

---

## Opioids: Public Health Issue

- Addiction: disrupting the positive feedback loop
  - Initial dose: exhilarating, but only with drug level threshold
  - Stopping:
    - Drug level drops
    - Toxins rise
    - Anxiety Centers: HYPER-RESPOND
    - Human Behavior .... Fixing problem is easy



Peterson, J. (2018) 12-Rules For Life: An Antidote to Chaos

---

---

---

---

---

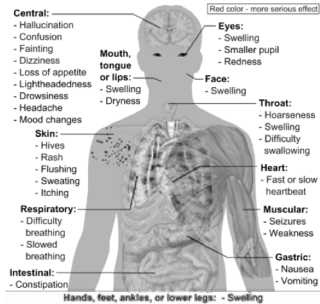
---

---

---



## Opioids: Why Avoid?



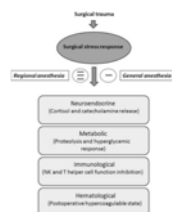
1. Tolerance
2. Dependence
3. Addiction

## What Can You Do?



## Goal: Opioid-Sparing

- Reduce Stress & Inflammation
  - Cortisol & Catecholamine release
- Optimize Immune Function
  - Natural Killer & T-Cell Function
- **Spare Opioids maximally**
- Reduce Symptom Burden
  - Rapid Rescue where prudent





## The Evidence

### Opioid-induced hyperalgesia: Cellular and molecular mechanisms

Laurie-Anne Roeckel, Glenn-Marie Le Coz, Claire Gavériaux-Ruff and Frédéric Simonin  
Neuroscience, 2016-12-03, Volume 338, Pages 160-182, Copyright © 2016 IBRO

---

---

---

---

---

---

---

## The Evidence

### Opioid-induced hyperalgesia: Cellular and molecular mechanisms

The Mechanism of **Hyperalgesia** and Anxiety Induced by Remifentanyl: Phosphorylation of GluR1 Receptors in the Anterior Cingulate Cortex  
by Jie Zeng; Sisi Li; Chao Zhang; [See more...](#)

Journal of Molecular Neuroscience, 05/2018

---

---

---

---

---

---

---

## The Evidence

### Opioid-induced hyperalgesia: Cellular and molecular mechanisms

The Mechanism of **Hyperalgesia** and Anxiety Induced by Remifentanyl: Phosphorylation of GluR1 Receptors in the Anterior Cingulate Cortex  
by Jie Zeng; Sisi Li; Chao Zhang; [See more...](#)

Increased **Hyperalgesia** and Proinflammatory Cytokines in the Spinal Cord and Dorsal Root Ganglion After Surgery and/or Fentanyl...  
by Chang, Lu; Ye, Fang; Luo, Quehua; [See more...](#)

---

---

---

---

---

---

---



## The Evidence

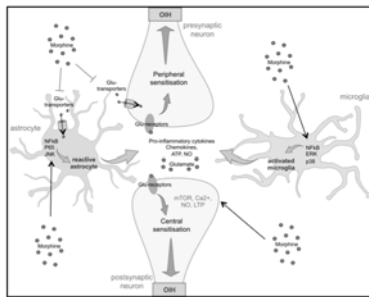
### Opioid-induced hyperalgesia: Cellular and molecular mechanisms

The Mechanism of **Hyperalgesia** and Anxiety Induced by Remifentanyl: Phosphorylation of GluR1 Receptors in the Anterior Cingulate Cortex  
by Jie Zeng; Sisi Li; Chao Zhang; See more...

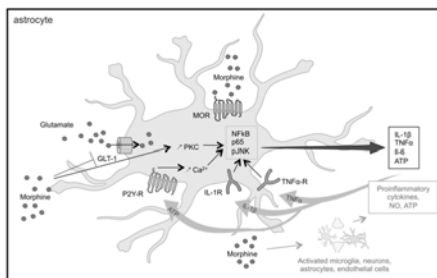
Increased **Hyperalgesia** and Proinflammatory Cytokines in the Spinal Cord and Dorsal Root Ganglion After Surgery and/or Fentanyl...  
by Chang, Lu; Ye, Fang; Luo, Quehua; See more...

### Remifentanyl-induced postoperative hyperalgesia: current perspectives on mechanisms and therapeutic strategies

Local and Regional Anesthesia, 2018;Volume 11:15-23



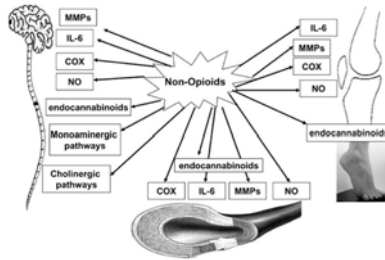
Yi, P., & Przybykowski, P. (2015). Opioid induced hyperalgesia. *Pain Medicine*, 16(5), S32-S36. doi:10.1111/pme.12914



Yi, P., & Przybykowski, P. (2015). Opioid induced hyperalgesia. *Pain Medicine*, 16(5), S32-S36. doi:10.1111/pme.12914



## Opioid-Sparing: Underlying Premise



Hamza, M., & Dionne, R. A. (2009). Mechanisms of Non-Opioid Analgesics Beyond Cyclooxygenase Enzyme Inhibition. *Current Molecular Pharmacology*, 2(1), 1–14.

## Opioid-Sparing: Underlying Premise

### Endogenous Chemicals Causing Pain

5-HT = 5-hydroxytryptamine  
 5-HT1AR = 5-hydroxytryptamine 1A receptors  
 5-HT2AR = 5-hydroxytryptamine 2A receptors  
 CB2R = cannabinoid CB2 receptors  
 CCK-8 = cholecystokinin octapeptide  
**COX-2 = cyclooxygenase-2**  
**CRF = corticotrophin-releasing factor**  
**GABA = γ-aminobutyric acid**  
 GDNF = glial cell line-derived neurotrophic factor  
 GFRα-1 = GDNF family receptor α-1  
 IAM-1 = intracellular adhesion molecule-1

**IL-6 = interleukin-6**  
**IL-1β = interleukin-1β**  
**NK-1 = neurokinin-1**  
 N/OFQ = nociceptin/orphanin FQ  
 p38 MAPK = p38 mitogen-activated protein kinase  
**PGE2 = prostaglandinE2**  
 p-GluN1 = phosphorylated GluN1  
**TNF-α = tumor necrosis factor-α**  
 TRPV1 = transient receptor potential cation channel subfamily V member 1  
**VIP = vasoactive intestinal polypeptides**



Hamza, M., & Dionne, R. A. (2009). Mechanisms of Non-Opioid Analgesics Beyond Cyclooxygenase Enzyme Inhibition. *Current Molecular Pharmacology*, 2(1), 1–14.

## Inflammation: Tumorigenesis

- **Immunoediting:** tumor cell eradication by immune system

1. **Elimination:** non-self >>> destroy
2. **Equilibrium:** tumor – antitumor balance
3. **Escape:** immune suppression >>> imbalance



## Inflammation: Tumorigenesis

- Surgery Causes:
  - Tissue Damage
  - Severe Pain
  - Immunosuppression (Profound)
  - Postoperative cancer recurrence

---

---

---

---

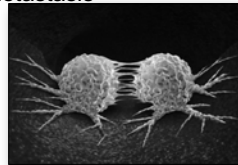
---

---

---

## Opioids

- Contribute to:
  - Promoting Inflammation
  - Impaired Immune Function
  - Contribute to Cancer Metastasis



Impact of perioperative pain management on cancer recurrence: an ASRA/ESRA special article

Andres Miscal, <sup>1,2</sup> Juan Pablo Catta, <sup>2</sup> Gina Votta-Vellis, <sup>4</sup> Mark Johnson, <sup>3</sup> Alain Borgeret, <sup>4</sup> Mohammed Touraine, <sup>2</sup> Vijay Guttumakkula, <sup>1</sup> Donald Buggy, <sup>3</sup> Ricardo Vallejo, <sup>2</sup> Esther Benedetti de Mampieri, <sup>1,2</sup> Dan Sessler, <sup>1,2</sup> Marc A. Hurlbourn, <sup>1,2</sup> Jose De Andres, <sup>1,2</sup> Oscar De Leon-Castillo <sup>1,2</sup>

---

---

---

---

---

---

---

## Inflammation: Tumorigenesis

- Inflammatory Mechanism causes:
  1. Nuclear transcription factor (NF- $\kappa$ B) release
  2. IL-6, IL-1 $\beta$ , TNF- $\alpha$
  3. Angiogenic factors (VEGF)
  4. COX-2
  5. Src gene activation (tumor promotion)

**\* May play a role in tumor progression and metastasis**

Mantovani A, Allavena P, Sica A, et al. Cancer-related inflammation. *Nature* 2008;454:436-44.  
 O'Leary DP, O'Leary E, Foley N, et al. Effects of surgery on the cancer stem cell niche. *Eur J Surg Oncol* 2010;42:319-25.  
 Piepeler T, Votta-Vellis EG, Liu G, et al. Antimetastatic potential of amide-linked local anesthetics: Inhibition of lung adenocarcinoma cell migration and inflammatory response independent of sodium channel blockade. *Anesthesiology* 2012;117:568-80.

---

---

---

---

---

---

---





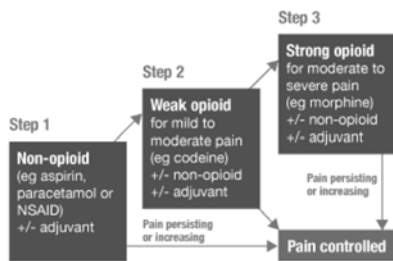


## Role of Opioids

- Promotes:
  - Angiogenic stimulus for tumor vascularization
  - Increase in VEGF, Src Gene Activation
  - Increased NOS, NO, COX-2
  - Increased metastasis (solid tumors)
    - MOR expression in **lung cancer** contributes to metastasis
- *silencing* the expression of the  **$\mu$ -opioid receptor (MOR)** in lung cancer cells **inhibits lung metastasis** by about **75%**.

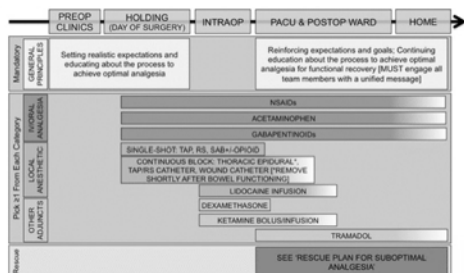
Matthew B. Lennon FE, Siegler J, et al. The novel role of the mu opioid receptor in lung cancer progression: a laboratory investigation. *Anesth Analg* 2011;112:558-67.

## Opioid-Sparing: Framework



WHO Analgesic Ladder. Retrieved from <http://www.paineurope.com/tools/who-analgesic-ladder>

## Opioid-Sparing: Innovation

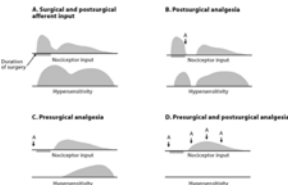


Scott et al., (2017) Retrieved from: <https://perioperativemedicinejournal.biomedcentral.com/articles/10.1186/s13741-017-0063-6>



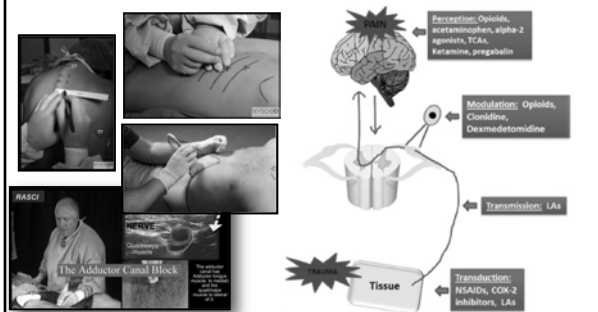
## Opioid-Sparing: Theory

- **Regional Anesthesia**
  - Controversy M & M
- **Pre-emptive Analgesia**
  - Prevent “pain” sensitization
  - Controversy
    - Regional Anesthesia
    - Agents?
    - Research: Poor!

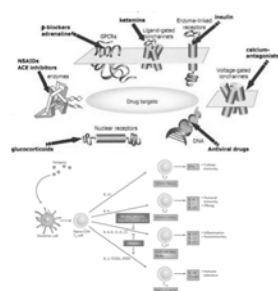


Guttschalk & Smith. (2007). New concepts in acute pain therapy: Preemptive analgesia. *Anaesthesia*, 62(10), 1579-84.

## Opioid-Sparing: Innovation



## Opioid-Sparing: Theory

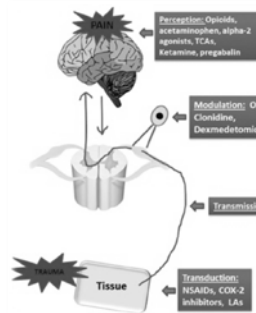


- **Pharmacological Agents**
  - Receptor Model Theory
    - Ionic Channels
    - Opioid/mu
    - GABA
    - NMDA
    - Adrenergic
    - Muscarinic
  - Modulation & Feedback
    - Agonist/Antagonists
    - Transporter Proteins
    - Synergism Theory

Korolik & Blum, (2014). RD/REB & PDB nuclear receptors as drug targets. *Nature Reviews Drug Discovery*, 13, 192-210.



## Opioid-Sparing: Innovation



- Lidocaine
- Gabapentinoids
- NSAIDs
- COX-2 Inhibitors
- Acetaminophen
- TCAs & SSRI
- Magnesium

---

---

---

---

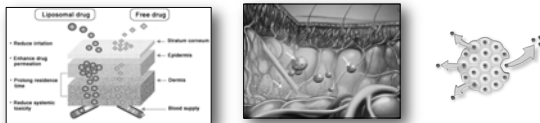
---

---

---

---

## Liposomal Bupivacaine: Background




---

---

---

---

---

---

---

---

## Medication Dosing

- Liposomal Bupivacaine 266mg/20ml (13.3mg/ml)
- Dilute: up to 280ml sterile saline (300 ml Total)
  - With Free Bupivacaine: < 50% Liposomal Dose
  - Typical total volume 40ml to 60ml

**"Bupivacaine HCl may be administered immediately before EXPAREL or admixed in the same syringe, as long as the ratio of the milligram dose of free bupivacaine HCl to EXPAREL does not exceed 1:2"**

---

---

---

---

---

---

---

---



## Bupivacaine Comparison

### Liposomal

- Onset: 5 minutes
- Peak Onset:
  - 30-120 minutes
- Half-Life: **24-34 Hours**
- Duration:
  - 24 Hours (Local) & 96 Hours (Systemic)

### Free

- Onset: 5-10 minutes
- Peak Onset:
  - 30-45 minutes
- Half-Life: **3.5 Hours**
- Duration:
  - 6-8 Hours

---

---

---

---

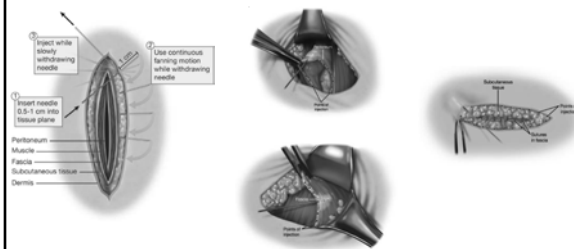
---

---

---

---

## Surgical Wound Infiltration



Joshi, G. P., Janis, J. E., Haas, E. M., Ramshaw, B. J., Nihira, M. A., & Quinlan, B. J. (2016). Surgical Site Infiltration for Abdominal Surgery: A Novel Neuroanatomical-based Approach. *Plastic and Reconstructive Surgery Global Open*, 4(12), e1161. <http://dx.doi.org/10.1097/GOX.0000000000001161>

---

---

---

---

---

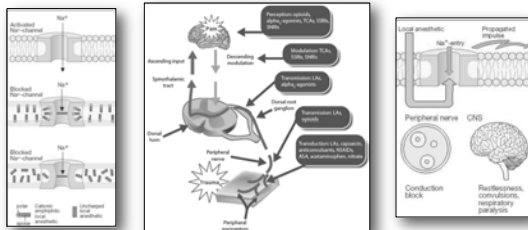
---

---

---

## Lidocaine Infusion

Infusion: 2mg/minute




---

---

---

---

---

---

---

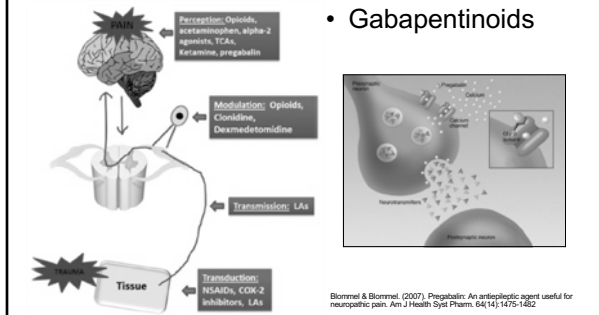
---





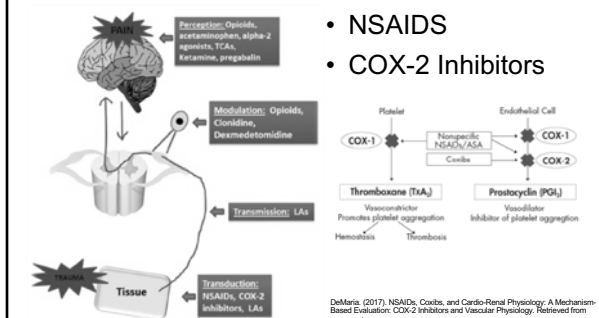


## Opioid-Sparing: Innovation



- Gabapentinoids

## Opioid-Sparing: Innovation



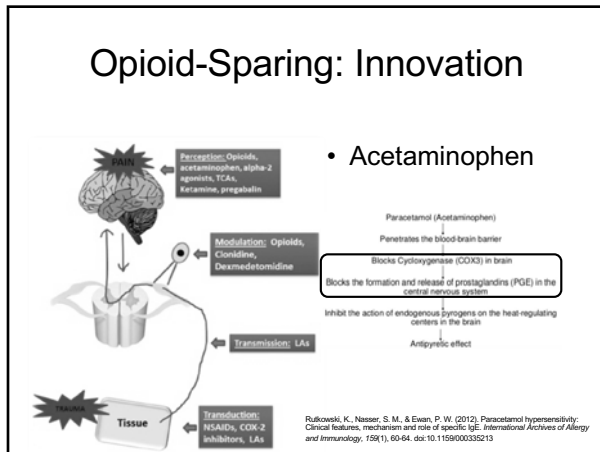
- NSAIDs
- COX-2 Inhibitors

## NSAIDs and COX-2 Inhibitors

- Reduce COX-2 and prostaglandins
- Breast Cancer & Colon Cancer
  - Reduced metastatic cancer: breast surgery
    - 20% Relative/10% Absolute reduction
  - Aspirin reduced metastatic colon cancer
  - COX-2 reduction
    - Decreased lung adenocarcinoma

Muscat JE, Chen SQ, Richie JP, et al. Risk of lung carcinoma among users of nonsteroidal antiinflammatory drugs. Cancer 2003;97:1732-6.  
 Schreinemachers DM, Everson RB. Aspirin use and lung, colon, and breast cancer incidence in a prospective study. Epidemiology 1994;5:138-46.  
 Harris RE, Beebe-Dunk J, Alshafie GA. Reduced risk of human lung cancer by selective cyclooxygenase 2 (cox-2) blockade: Results of a case control study. Int J Biol Sci 2007;3:329-34.






---

---

---

---

---

---

---

---

### Acetanilide Derivative (Acetaminophen)

1000mg IV Q6Hours

- Pharmacodynamic Profile
- IV is Superior: Why?
  - IV 70% Availability

***Res ipsa loquitur***

---

---

---

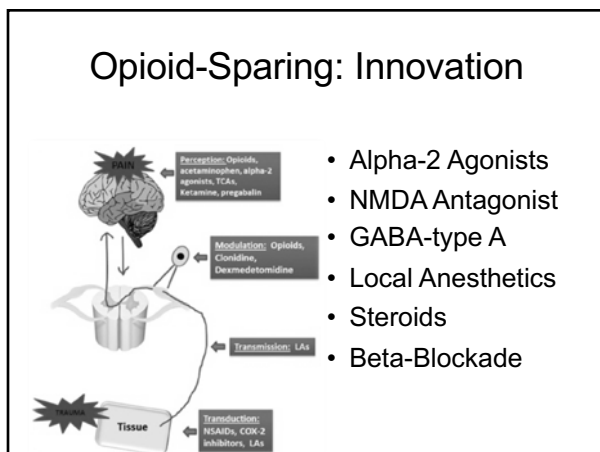
---

---

---

---

---




---

---

---

---

---

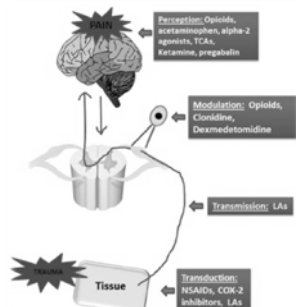
---

---

---



## Opioid-Sparing: Innovation



- Alpha-2 Agonists

The diagram illustrates the pain pathway with four stages: Perception (brain), Modulation (spinal cord), Transmission (nerve), and Transduction (tissue). Various drugs are shown acting at these stages: Opioids, tricyclic antidepressants, and alpha-2 agonists at perception; Opioids, clonidine, and dexmedetomidine at modulation; Local anesthetics at transmission; and NSAIDs, COX-2 inhibitors, and local anesthetics at transduction.

---

---

---

---

---

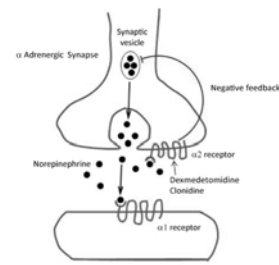
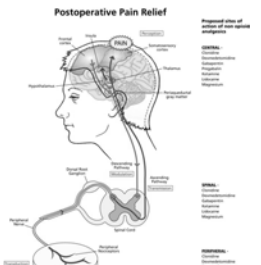
---

---

---

## Alpha-2 Agonist (Clonidine, Dexmedetomidine)

(Infusion: 0.3 mcg/Kg/Hr)

The left diagram shows an alpha-2 adrenergic synapse where norepinephrine release is inhibited by negative feedback from alpha-2 receptors. The right diagram illustrates postoperative pain relief through central and peripheral mechanisms, including analgesia, sedation, and anxiolysis.

---

---

---

---

---

---

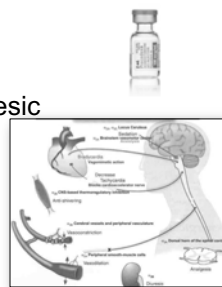
---

---

## Alpha-2 Agonist (Clonidine, Dexmedetomidine)

Infusion: 0.3 mcg/Kg/Hr

- anti-hypertensive effect
- sedative, anxiolytic, analgesic – **Modulation Pain Pathway**
- side effects:
  1. Bradycardia
  2. Hypotension
  3. Sedation



The diagram shows clonidine acting on alpha-2 receptors in the brain to modulate pain and on the heart to cause bradycardia and hypotension.

---

---

---

---

---

---

---


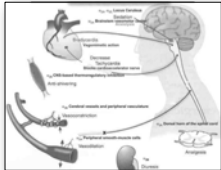
---



## Alpha-2 Agonist (Clonidine, Dexmedetomidine)

*Infusion: 0.3 mcg/Kg/Hr*

- Analgesic, sedative
  - Not studied to date for immune modulation

---

---

---

---

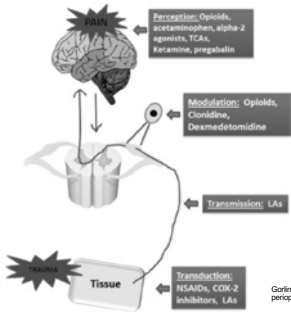
---

---

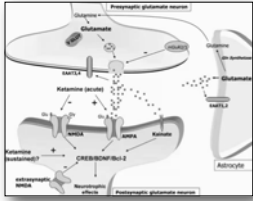
---

---

## Opioid-Sparing: Innovation



- NMDA Antagonist



Gorlin AW, Rosenfeld DM, Ramakrishna H. Intravenous sub-anesthetic ketamine for perioperative analgesia. *J Anesth Res Clin Pharmacol* 2016;32:165-7

---

---

---

---

---

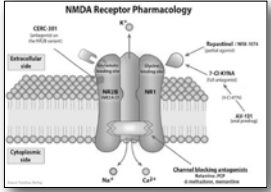
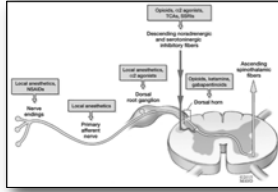
---

---

---

## NMDA Receptor Antagonist (Ketamine)

*Infusion: 10 mg/Hr*

---

---

---

---

---

---

---

---

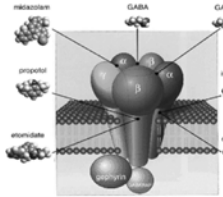






## Sedative Hypnotic (Propofol)

Infusion: 25-150 mcg/Kg/minute




---

---

---

---

---

---

---

---

## Traditional Methodology: Direct Cost

Drug	Cost per Unit	Units	Total Cost
Midazolam	\$2.40	1	\$2.40
Famotidine	\$2.53	1	\$2.53
Sufentanil	\$8.00	3	\$24.00
Propofol	\$2.30	1	\$2.30
Cis-Atracurium	\$24.40	3	\$73.20
Glycopyrrolate	\$46.75	1	\$46.75
Neostigmine	\$52.85	1	\$52.85
Desflurane	\$6.99	6	\$41.94
Crystalloid	\$1.95	3	\$5.85
Ondansetron	\$0.70	2	\$1.40
Bupivacaine	\$36.64	1	\$36.64
Hydromorphone	\$8.08	1	\$8.08
<b>Total Cost</b>			<b>\$297.94</b>




---

---

---

---

---

---

---

---

## ERAS Methodology: Direct Cost (The Alternative)

Drug	Cost per Unit	Units	Total Cost
Gabapentin	\$12.00	1	\$12.00
Celebrex	\$4.15	1	\$4.15
Tramadol	\$7.35	1	\$7.35
Acetaminophen	\$35.40	3	\$106.20
Alvimopan	\$700.00	1	\$700.00
Dexmedetomidine	\$31.92	1	\$31.92
Propofol	\$2.30	9	\$20.70
Ketamine	\$21.24	1	\$21.24
Lidocaine 0.4%	\$2.53	1	\$2.53
Albumin 5%	\$83.72	3	\$251.16
Glycopyrrolate	\$46.75	1	\$46.75
Neostigmine	\$52.85	1	\$52.85
Crystalloid	\$1.95	1	\$1.95
Ondansetron	\$0.70	2	\$1.40
Bupivacaine	\$36.64	1	\$36.64
Liposomal Bupivacaine	\$285.00	1	\$285.00
Hydromorphone	\$8.08	1	\$8.08
<b>Total Cost</b>			<b>\$1,428.30</b>




---

---

---

---

---

---

---

---



### Variable Cost of Adverse Drugs Events (ADE)

- PONV
- Ileus
- Respiratory Depression
- Immobility/DVT
- Urinary Retention
- Mental Status Change
- Increased LOS
- 30 Day Readmission

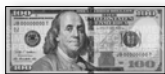


## Post-Operative Nausea & Vomiting (PONV)



## Post-Operative Nausea & Vomiting (PONV)

- **15%-33% occurrence** surgical outpatients
- Adjusted **incremental cost \$75** (95% CI - \$67-\$86) per patient
  - **\$87.12 per patient** today
- Average **Delayed Discharge** by 60 minutes (234 min. versus 171 min.)
- **Lasting Effects:** up to 72 hours
- **Quality of Life:** lower for PONV – **The Intangible!**
  - Only 49% rate 1 for PONV versus 94% rated 1 for POD 1 to 3
    - Most Patients experiencing PONV at 72 hours



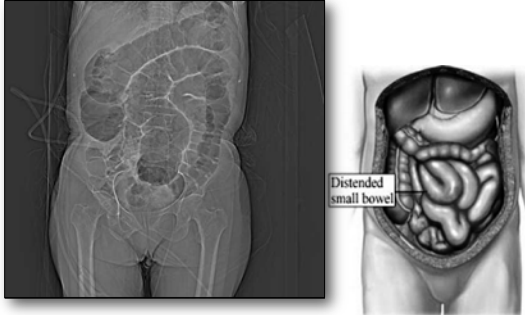
Can. J. Anaesth./Can. Anaesth. (2002) 49:366-371  
DOI: 10.1007/s00540-001-0004-4

REPORTS OF ORIGINAL INVESTIGATIONS

**A time-motion economic analysis of postoperative nausea and vomiting in ambulatory surgery**  
Ivan Parra-Sanchez, MD • Rania Abdallah, MD • Jing You, MS • Alex Z. Fu, PhD • Martin Grady, MD • Kenneth Cummings III, MD • Christian Apfel, MD • Daniel L. Sessler, MD



## Post-operative Ileus (POI)




---

---

---

---

---

---

---

---

## Post-Operative Ileus (POI)

- **Occurrence:** 10-40% in patients undergoing Radical Cystectomy
  - **Average Occurrence Rate:** 15.6%
  - POI Contributes to 50-70% of all complications
  - **Increases LOS:** mean of **4 days** (Range: 3-10 days)
    - **Doubles the cost** of Hospital Stay
  - **Cause:** Opioid binding to gastrointestinal mu-receptors
  - Additional **Overall Cost** due to POI: **\$10,246.00 per event**

- **Prevention:** Alvimopan which binds to gastrointestinal mu-receptors
- **Direct Cost:** \$700 per hospital stay
- **Results:** 50% Rate Reduction in POI to 7.8%

Alvimopan for prevention of postoperative paralytic ileus in radical cystectomy patients: a cost-effectiveness analysis  
William M. Altman, Neil Lohani\*, Dipan J. Parekh, Joseph M. Bunker and Richard S. Smith  
University of Texas Health Science Center San Antonio, San Antonio, and \*University of Texas Southwestern Medical Center, Dallas, TX, USA

---

---

---

---

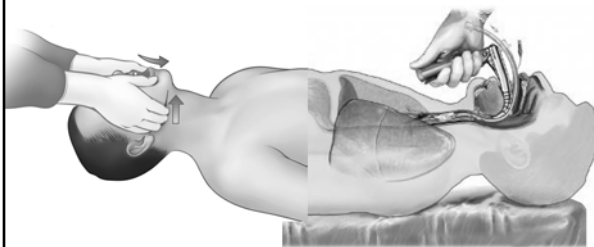
---

---

---

---

## Respiratory Depression: ORAE




---

---

---

---

---

---

---

---



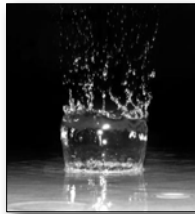
## Respiratory Depression:

- N = **319,898**
- Incidence: **3.3%** (12.2% Overall)
- Cost: **\$155.33 per patient**
- LOS: **3.3 Days**
- 30-Day Readmission: 6.4%

PHARMACOECONOMICS AND OUTCOMES IN PAIN AND  
PALLIATIVE CARE  
Gary M. Oskow, Tong J. Guo, Bernadette H. Johnson, and Scott B. Robinson  
Effect of Opioid-Related Adverse Events on Outcomes in  
Selected Surgical Patients



## Post-Operative Urinary Retention (POUR)



## Postoperative Urinary Retention (POUR)

- **Occurrence: 2.1%**, based on the Surgical Care Improvement Project

- **Sample Size: 415,409** surgical patients
  - **Study: 43,030** developed POUR
    - POUR Contributed **9.2%** of Urinary Tract Infections
  - **Increases LOS:** mean of 1.1 days
- National incidence and outcomes of postoperative urinary retention in the Surgical Care Improvement Project

Alex K. Wu, M.D.<sup>a,\*</sup>, Andrew D. Auerbach, M.D.<sup>a</sup>, David S. Aaronson, M.D.<sup>a,b</sup>

<sup>a</sup>Department of Urology, University of California San Francisco, San Francisco, CA, USA; <sup>b</sup>Department of Urology, Kaiser Permanente Medical Group, Oakland, CA, USA



## Variable Cost Benchmarks




---

---

---

---

---

---

---

## Incidence: Variable Cost Per Episode

<u>Incidence</u>	Cost Per Episode	Probability
Respiratory Depression	\$568.00	3.30%
PONV	\$87.12	15.00%
Post-Operative Ileus	\$10,247.00	15.60%
Urinary Retention	\$1,357.00	2.00%
Mental Status Change	\$2,500.00	15.00%
DVT	\$4,159.00	2.20%
<b>30-Day Readmission</b>	<b>\$11,200.00</b>	5.40%
Length of Stay	\$2,064.00/Day	10.0 Days

---

---

---

---

---

---

---

## Cost Benefit & Cost Effectiveness

**A Factor of 5.6**

<u>Traditional Strategy</u>	<u>Incidence</u>	<u>Opioid-Sp</u>
8.00%	Pruritus	<b>0.00%</b>
3.30%	Respiratory Depression	<b>0.00%</b>
15.00%	PONV	7.50%
15.60%	Post-Operative Ileus	7.80%
2.00%	Urinary Retention	<b>0.00%</b>
15.00%	Mental Status Change	3.00%
2.20%	DVT	1.00%
5.40%	30-Day Readmission	<b>0.00%</b>
10.0 Days	Length of Stay	<b>7.00 Days</b>
<b>\$1,379.38</b>	Cost Per Episode (Probability)	<b>\$247.69</b>

---

---

---

---

---

---

---



## Summary

- Public Health: Opioid Pandemic
- Opioid Crisis
- Non-Opioid Framework
- Non-Opioid Premise
- Non-Opioid Theory
- Non-Opioid Techniques
- Opioid Rescue

---

---

---

---

---

---

---