Objectives:

- 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
- Describe the cost-savings opioid sparing techniques generate for hospital systems through a sensitivity analysis
- Translate the economic impact opioid sparing techniques make on the opioid crisis.

The Issue

Persistent opioid use after surgery affects millions of Americans:

- More than **2 million people** may transition to persistent opioid use following elective, ambulatory surgery each year. [1]
- Overprescribing of postsurgical opioids results in **billions of unused pills**. [2]
- In 2015, **2.1 million people** misused prescription opioids for the first time. [3]
- **Nearly half** of all U.S. opioid overdose deaths involve a prescription opioid. [4]

Opioids: Why Avoid?

1. Tolerance
2. Dependence
3. Addiction
4. Harm*

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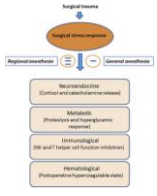
Opioid-Sparing

- Reduce Stress & Inflammation
  - Cortisol & Catecholamine release
- Optimize Immune Function
  - Natural Killer & T-Cell Function
- **Spare Opioids maximally**
- Reduce Symptoms Burden
  - Rapid Rescue where prudent: Sparing Not Free



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

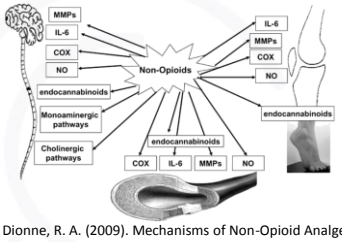
Journal of Molecular Neuroscience, 05/2018

The Evidence

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...

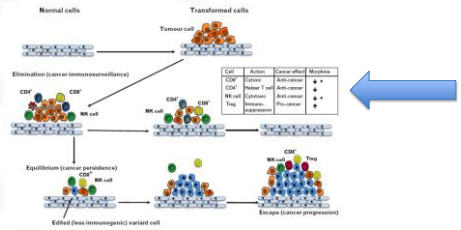
Remifentanil-induced postoperative hyperalgesia: current perspectives on mechanisms and therapeutic strategies
Local and Regional Anesthesia. 2018;Volume 11:15-23

Opioid-Sparing: Underlying Premise



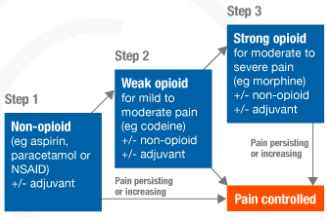
Hamza, M., & Dionne, R. A. (2009). Mechanisms of Non-Opioid Analgesics Beyond Cyclooxygenase Enzyme Inhibition. *Current Molecular Pharmacology*, *2*(1), 1–14.

Why Avoid Opioids?



Wigmore, T., & Farquhar-Smith, P. (2016). Opioids and cancer: Friend or foe? *Current Opinion in Supportive and Palliative Care, 10*(2), 109-118. doi:10.1097/SPC.0000000000000208

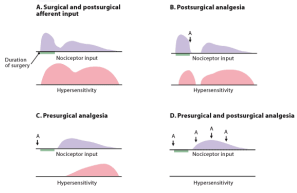
Opioid-Sparing: Framework



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

Opioid-Sparing: Theory

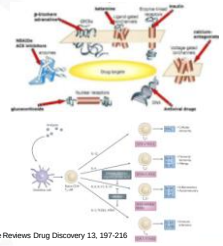
- Regional Anesthesia
  - Controversy M & M
- Pre-emptive Analgesia
  - Prevent "pain" sensitization
  - Controversy
    - Regional Anesthesia
    - Agents?
    - Research: Poor!



Gottschalk & Smith. (2001). New concepts in acute pain therapy: Preemptive analgesia. Am Fam Physician. 2001 May 15;63(10):1979-84.

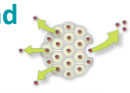
Opioid-Sparing: Innovation

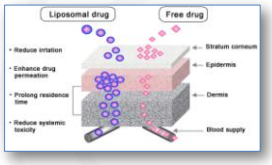
- **Pharmacological Agents**
  - Receptor Model Theory
    - Ionic Channels
    - Opioid/mu
    - GABA
    - NMDA
    - Adrenergic
    - Muscarinic
  - Modulation & Feedback
    - Agonist/Antagonists
    - Transporter Proteins
    - Synergism Theory

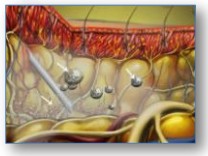


Kojetin & Burris. (2014). REV-ERB & ROR nuclear receptors as drug targets. Nature Reviews Drug Discovery 13, 197-216

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

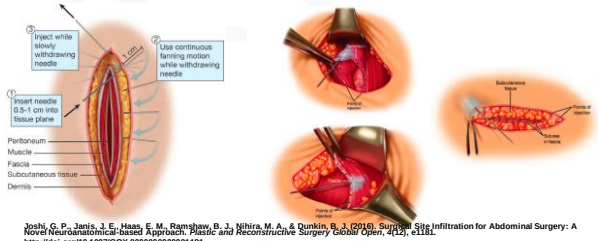
Liposomal

- 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

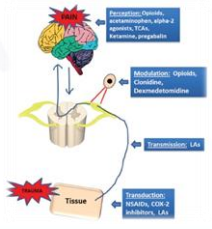
Surgical Wound Infiltration



Joshi, G. P., Janis, J. E., Haas, E. M., Ramshaw, B. J., Nihira, M. A., & Dunkin, B. J. (2016). Surgical Site Infiltration for Abdominal Surgery: A Novel Neuroanatomical-based Approach. *Plastic and Reconstructive Surgery Global Open*, 4(12), e1181. http://doi.org/10.1097/GOX.0000000000001181

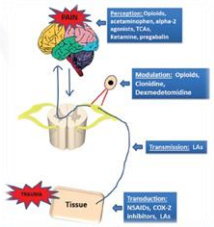
Opioid-Sparing: Innovation

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



Opioid-Sparing: Innovation

- Alpha-2 Agonists
- NMDA Antagonist
- GABA-type A
- Local Anesthetics
- Steroids
- Beta-Blockade



Enhanced Recover after Surgery

- **Enhanced Recovery after Surgery (ERAS)** is a patient-centered, evidence-based, pain management strategy employed by CRNAs to **reduce the need for opioids, improve patient outcomes and reduce costs**.

ERAS Pain Management Pathway

- **Preadmission** – patient/family education; recovery and pain management planning
- **Preoperative** – minimize fasting to reduce anxiety and pain perception and improve diet recovery
- **Intraoperative** – administer analgesics and nerve blocks for pain and nausea/vomiting management
- **Postoperative** – patient assessment, plan modification, and multimodal medication prescribing
- **Post-Discharge** – education on anesthesia recovery, surgical procedure and pain management
- **Continued Quality Improvement** – analysis of compliance and outcomes to improve care

Incidence: Variable Cost Per Episode

Incidence	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%
30-Day Readmission	$11,200.00	5.40%
Length of Stay	$2,064.00/Day	10.0%

Cost Benefits & Cost Effectiveness

A Factor of 5.6		
Traditional Strategy	Incidence	ERAS Strategy
8.00%	Pruritus	0.00%
3.30%	Respiratory Depression	0.00%
15.00%	PONV	7.50%
15.60%	Post-Operative Ileus	7.80%
2.20%	Urinary Retention	0.00%
15.00%	Mental Status Change	3.00%
2.20%	DVT	1.00%
5.40%	30-Day Readmission	0.00%
10.0 Days	Length of Stay	7.00 Days
$1,379.38	Cost Per Episode (Probability)	$247.69

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
			Total Cost: $297.94

ERAS Methodology: Direct Cost

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
			Total Cost: $1,428.30

Cost-Effective: ERAS

- ERAS provides an average savings of **$880 to $5,560** per patient. [5,6]
- ERAS reduces patient length of stay by **3-4 days** on average. [7-12]
- ERAS **reduces 30-day patient** readmission rates and costs. [13,14]
- ERAS **helps patients return** to normal activities more quickly. [6]

Summary

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

References

- 1. Brummett et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. JAMA Surg. 2017;152(6). e170504
- 2. United States for Non-Dependence. An Analysis of Opioid Overprescribing in America. QuintilesIMS Institute. Sept. 2017.
- 3. 2015 National Survey on Drug Use and Health (SAMHSA)
- 4. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; CDC 2016.
- 5. Schmidt et al., Accelerated Recovery Within Standardized Recovery Pathways After Esophagectomy. Ann Thorac Surg 2016;102:931–9;
- 6. Chipollini, J. et al., Cost Impact Analysis of Enhanced Recovery after Surgery Protocol Implementation in a Radical Cystectomy Cohort of Patients. The Journal of Urology 2017; 197(4), e414-e415. doi:10.1016/j.juro.2017.02.991
- Wick EC, Galante DJ, Hobson DB, et al. Organizational Culture Changes Result in Improvement in Patient-centered Outcomes
- Implementation of an Integrated Recovery Pathway for Surgical Patients. J Am Coll Surg 2015;221:669e677
- 8. Thiele et al., Standardization of Care: Impact of an Enhanced Recovery Protocol on Length of Stay, Complications, and Direct Costs after Colorectal Surgery. J Am Coll Surg 2015;220:430e443
- 9. Miller TE, Thacker JK, WhiteWD, et al. Reduced length of hospital stay in colorectal surgery after implementation of an enhanced recovery protocol. Anesth Analg 2014;118:1052e1061
- 10. Archibald LH, Ott MJ, Gale CM, et al. Enhanced Recovery after Colon Surgery in a Community Hospital System. Dis Colon Rectum 2011;54:840e845
- 11. Kariv Y, Delaney CP, Senagore AJ, et al. Clinical Outcomes and Cost Analysis of a "Fast Track" Postoperative Care Pathway for Ileal Pouch-anal Snastomosis: A Case Control Study. Dis Colon Rectum 2007;50:137e146
- 12. Stephen AE, Berger DL. Shortened Length of Stay and Hospital Cost Reduction with Implementation of an Accelerated Clinical Care Pathway after Elective Colon Resection. Surgery 2003;133: 277e282;
- 13. Schmidt et al., Accelerated Recovery Within Standardized Recovery Pathways After Esophagectomy Ann Thorac Surg 2016;102:931–9
- 14. Semerjian, A., et al. (2017). pd67-11 Enhanced Recovery after Radical Cystectomy Reduces Cost and Length of Stay: The Johns Hopkins Experience. The Journal of Urology 2017; 197(4), e1280-e1281. doi:10.1016/j.juro.2017.02.2987

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