Vermont Child Health Improvement Program
UNIVERSITY OF VERMONT LARNER COLLEGE OF MEDICINE

OB/GYN Webinar Series 2018-2019

Hot Topics in Obstetrical Care

Thursday, April 18th, 12:15pm- 1pm EST

Presented by:

The University of Vermont
LARNER COLLEGE OF MEDICINE

THE University of Vermont MEDICAL CENTER

VCHIP Webinars

Collaboration with UVMMC, Vermont Dept. of Health, VCHIP

All webinars are recorded @ vchipobstetrics.org

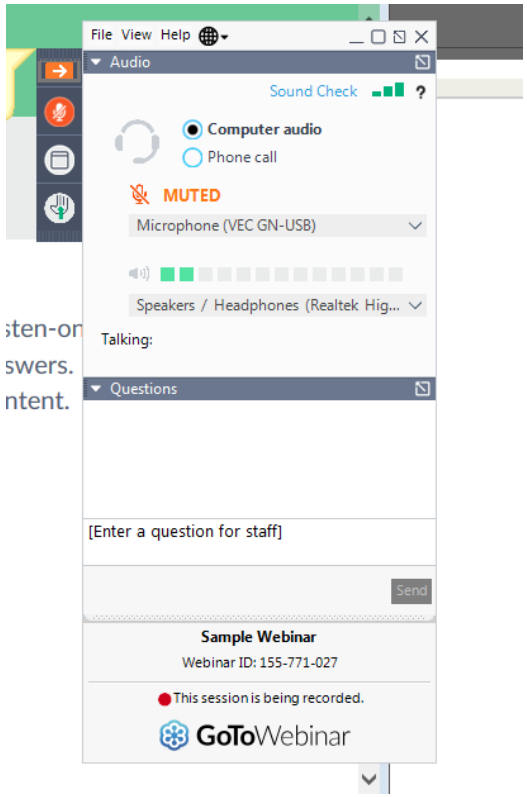
Upcoming Webinars:

- **May 14th, 2019 @ 12:15pm** Venous Thromboembolism and Pulmonary Embolism & VT Dept. of Health Topic
- **June 11, 2019 @ 12:15pm** Severe Maternal Morbidity & VT Dept. of Health Topic

Register at vchipobstetrics.org

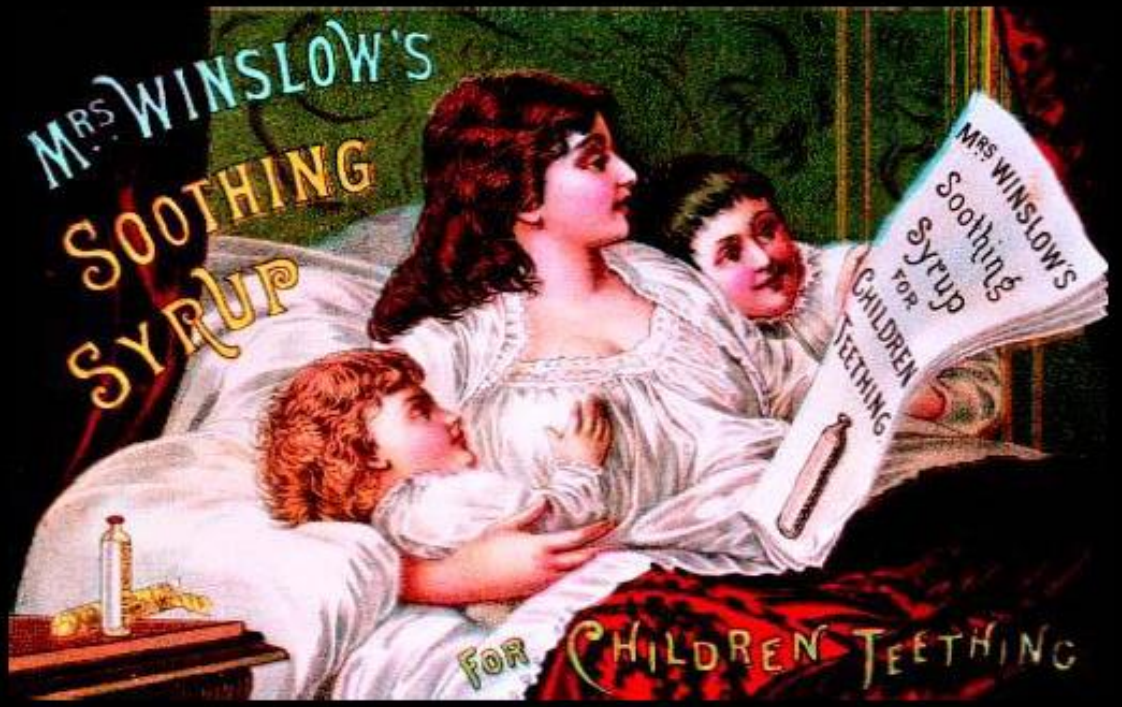
Questions/Comments During the Webinar

Use the Question box in your webinar toolbar



Sex, Drugs, and Pain: Intrapartum and postpartum pain control in the opioid maintained patient

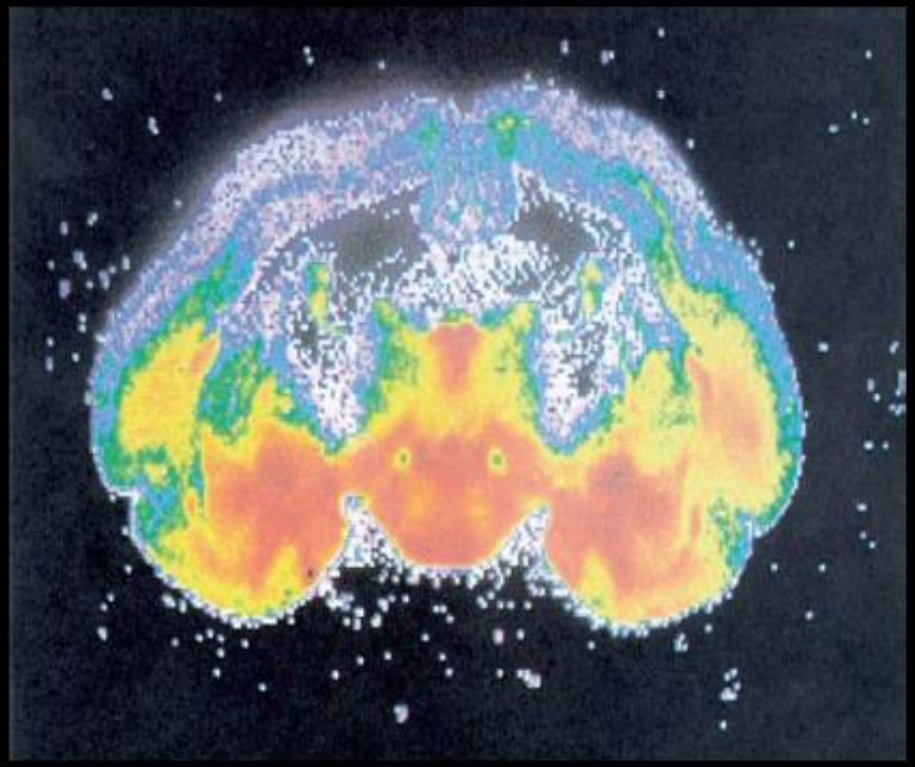
Marjorie Meyer MD
Associate Professor
Maternal Fetal Medicine
University of Vermont



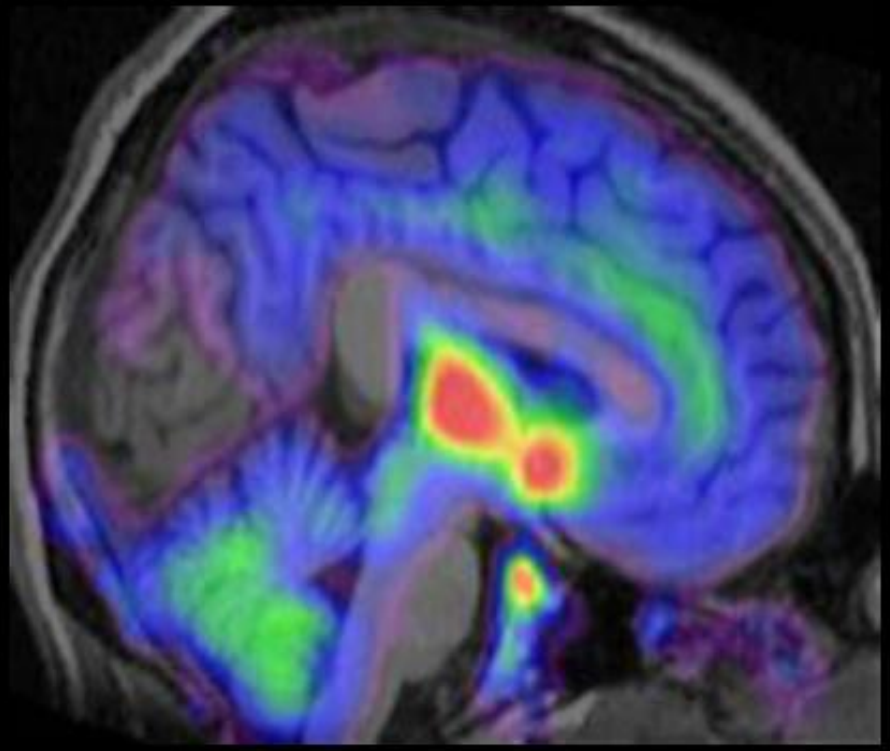
"Labor is a natural process necessarily attended with more or less violence……it involves exertion which is associated with more or less suffering…."

Barton Hirst MD, System of Obstetrics, 1888

Sex, drugs, and pain: different issues, same central processing



Guinea pig brain; red areas represent highest density, yellow areas represent moderate density, and blue, purple, and white represent low density of opioid receptors.



Human opioid receptors following smoking
www.med.umich.edu/opm/newspage/2004/smoking.htm

DuPen, 2007

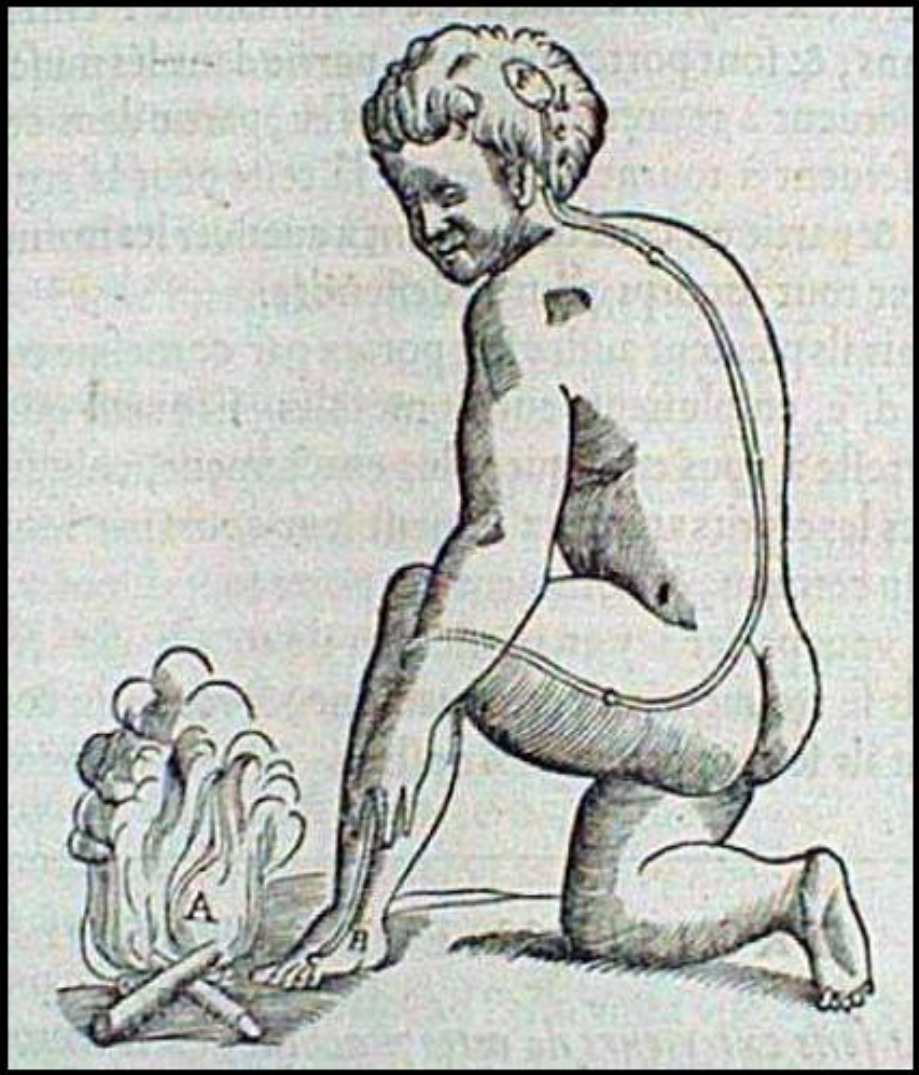
Pain is inextricably linked to action

I think, therefore I am….

- *Believed that only humans had minds; the body was mechanical, obeying the laws of physics; the mind was nonmaterial and acted through the body through the pineal gland.*

- *Not only does the mind control the body, but the body controls the mind (ie: actions performed out of passion)*

French philosopher Rene Descartes (1596-1650): the first mind-body practitioner



Objectives

- Review the etiology of pain: labor and surgical
- Review mechanisms of opioid tolerance and opioid induced hyperalgesia
- Review differences in response to intrapartum and postpartum pain in women receiving methadone or buprenorphine for opiate dependence
- Review a plan for pain management in the opioid dependent patient presenting for delivery

Classification of pain

- Nociceptive: damage to skin or peripheral tissue. Considered beneficial as it alerts individual to further injury. Post-operative pain.
  - Transmitted through normal sensory receptors via afferent neurons to the dorsal horn, up the ascending spinothalamic pathways to higher neural centers
  - Felt locally, not in a single dermatome

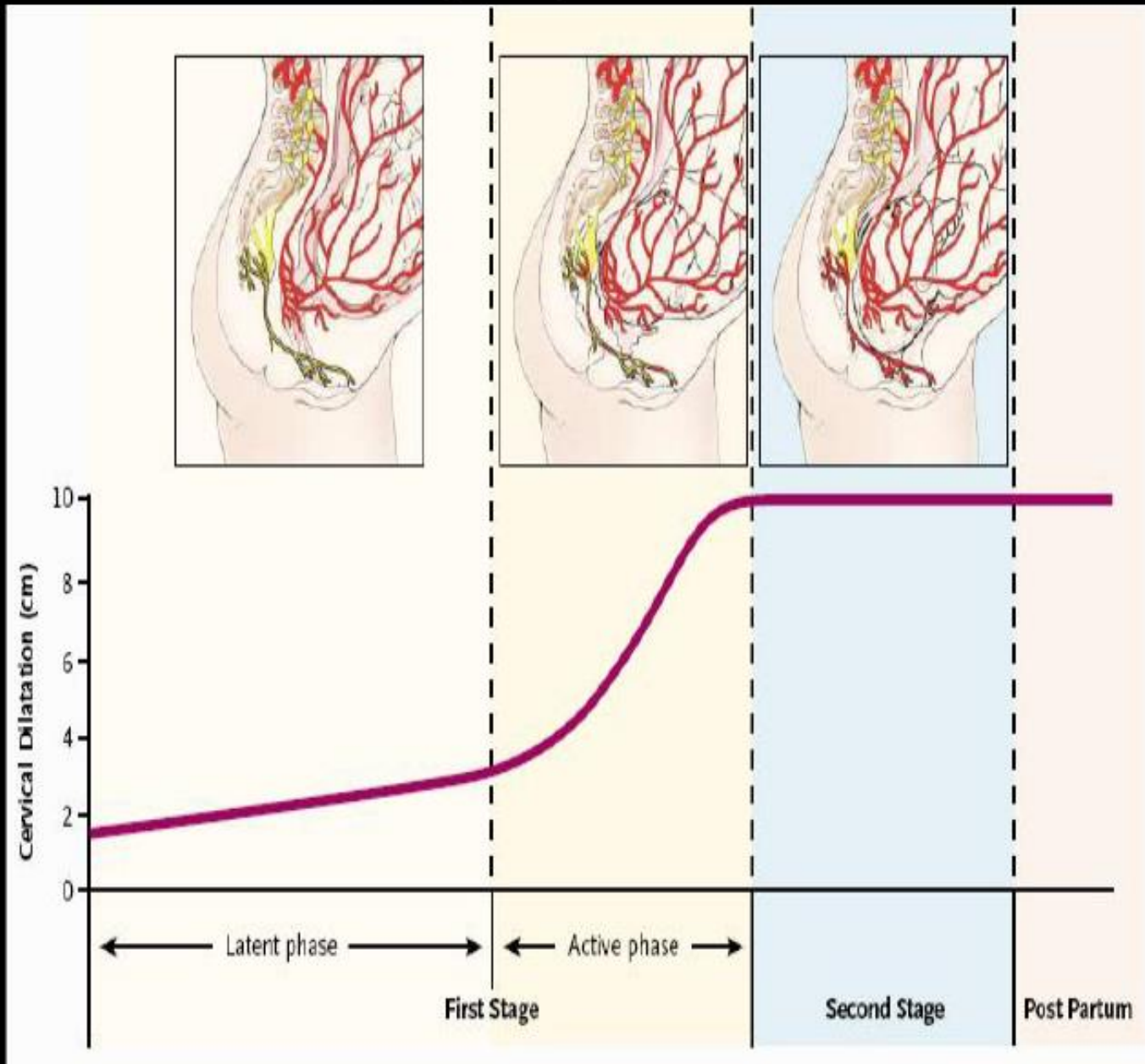
- Neuropathic: damage to some element of the nervous system such as peripheral nerve, nerve root, or spinal cord. Chronic pain.
  - Transmitted through usual pain fibers and the low threshold larger A fibers
  - Response is out of proportion to stimulus intensity
  - Allodynia: pain from a stimulus not normally painful
  - Hyperpathia: greater than normal pain sensation from a normally painful stimulus
  - Dysesthesias: painful paresthesias
  - Can be referred or dermatomal

Labor pain is nociceptive pain:

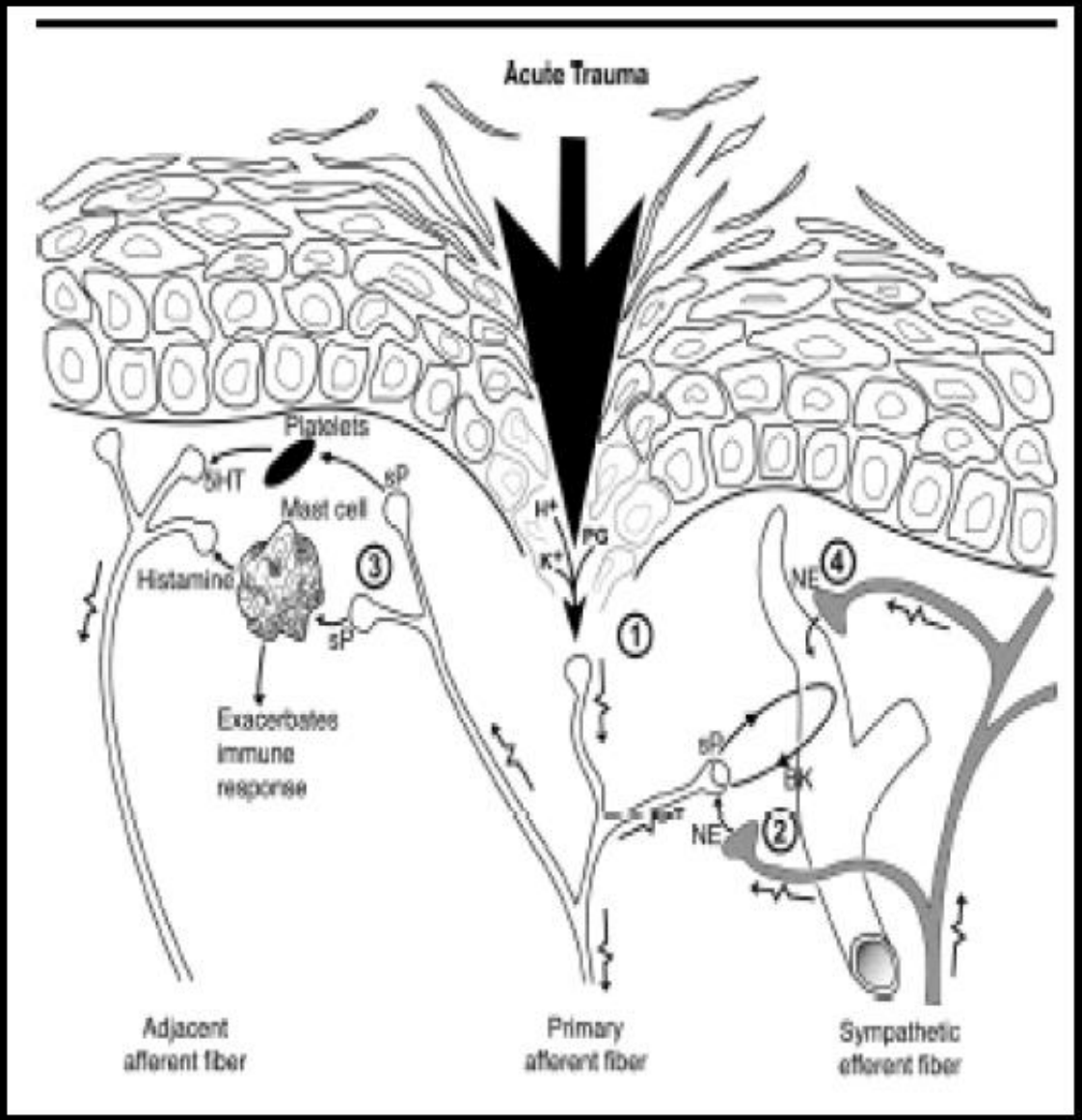
- Pain during the first stage of labor is visceral and is therefore mediated by the T10 through L1 segments of the spine
- during the later part of the first stage and throughout the second stage, an additional somatic component is present, mediated by the S1 through S4 segments of the spine.

NEJM, 2003

Labor pain:
Different pathways activated during labor progress:
Active pain pathways are marked in red.



Surgical pain is nociceptive pain:



Trauma releases K, 5HT, and histamine from damaged cells; bradykinin released from damaged vascular wall

Prostaglandins potentiate nociception

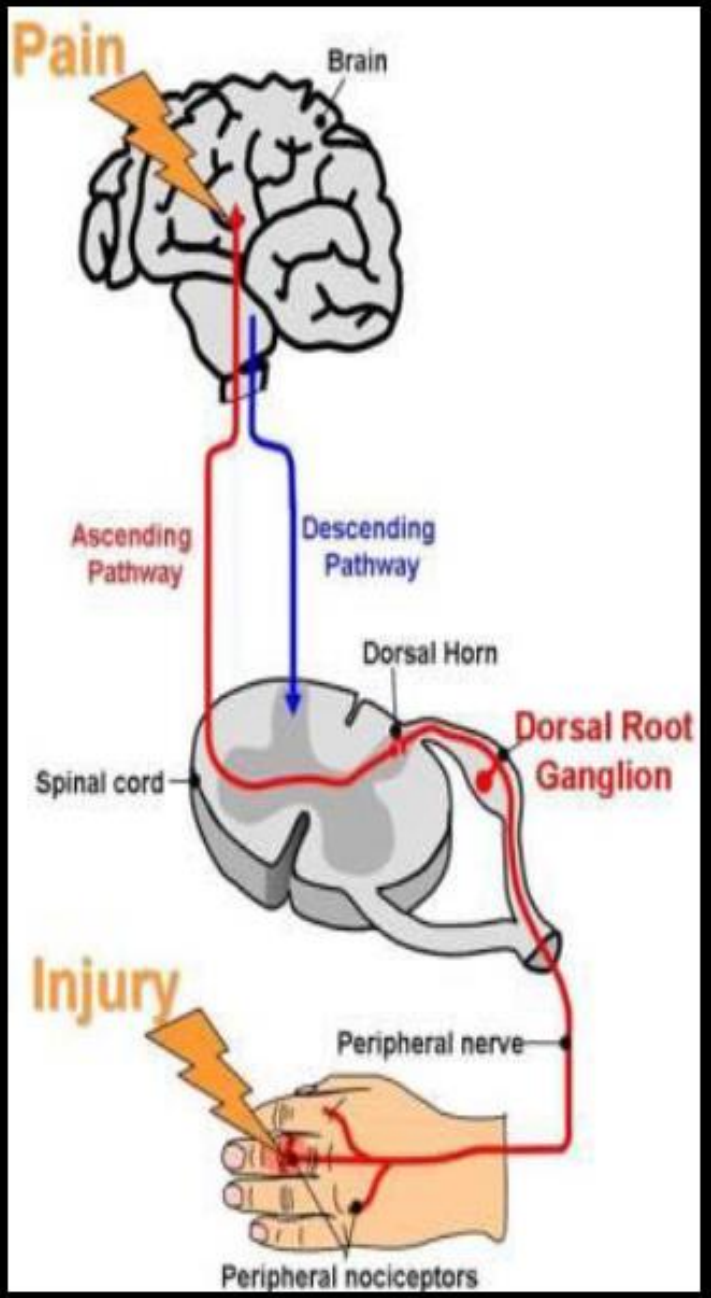
Substance P is released form the primary afferents and further potentiates histamine and bradykinin

Reflexes mediated by the sympathetic efferents sensitize nociception by further release of PG, BK, and local vasoconstriction

Pain modulation occurs at BOTH peripheral and central levels:

peripheral nociceptive pathway through the spinal cord dorsal neurons

Nociceptive signals are modulated locally, at the level of the spinal cord, in the brainstem, and higher cortical centers



Modulation can:

- Decrease the output (analgesia)
- Increase of gain in the system (hyperalgesia)
- Reduce the threshold (allodynia)

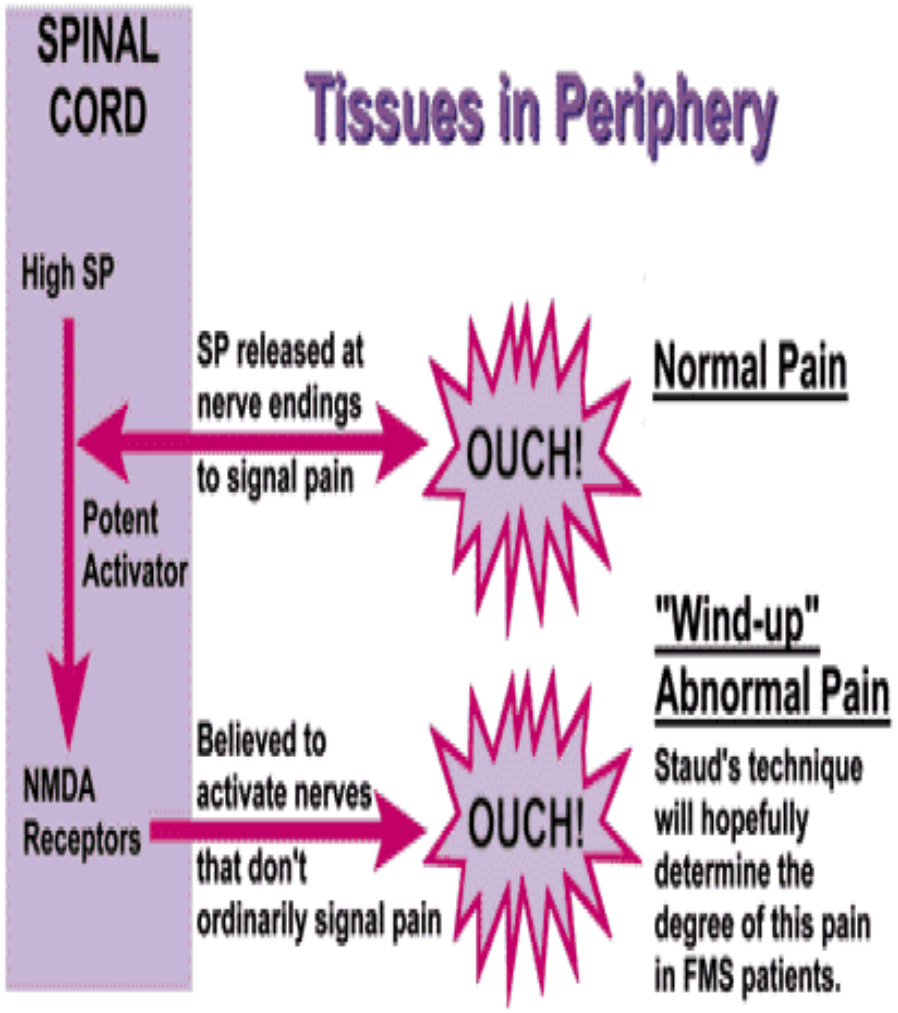
"Wind-up" accentuates the intensity of the pain signal (hyperalgesia and allodynia)

- Spinal facilitation: wind-up:
  - –the dorsal horn neurons fire more easily and keep firing

- <u>Role of the sympathetic nervous system:</u>
  - –new sympathetic nerve synapses develop after injury
  - –Increased sensitivity of the afferent (signaling) fiber

Once wind-up is initiated, higher doses of analgesics are required

It is more difficult to suppress the wind-up after it is established (ie: best to stay ahead of the pain)



Take home messages regarding pain associated with labor and delivery

- Labor, delivery, and operations hurt
- Nociceptive signals are processed through the dorsal horn of the spinal column
- Pain signals are modulated at each level and can be increased or decreased
- Opioids are abundantly located throughout the signaling pathway and modulate signal intensity: acute use generally inhibitory, chronic use can increase pain signaling
- AMPA and NMDA receptors can wind-up the signal intensity, interacting with the sympathetic nervous system, to increase the pain signal and can create pain that is difficult to treat

Opiate agonist medications used for the treatment of opiate dependence:

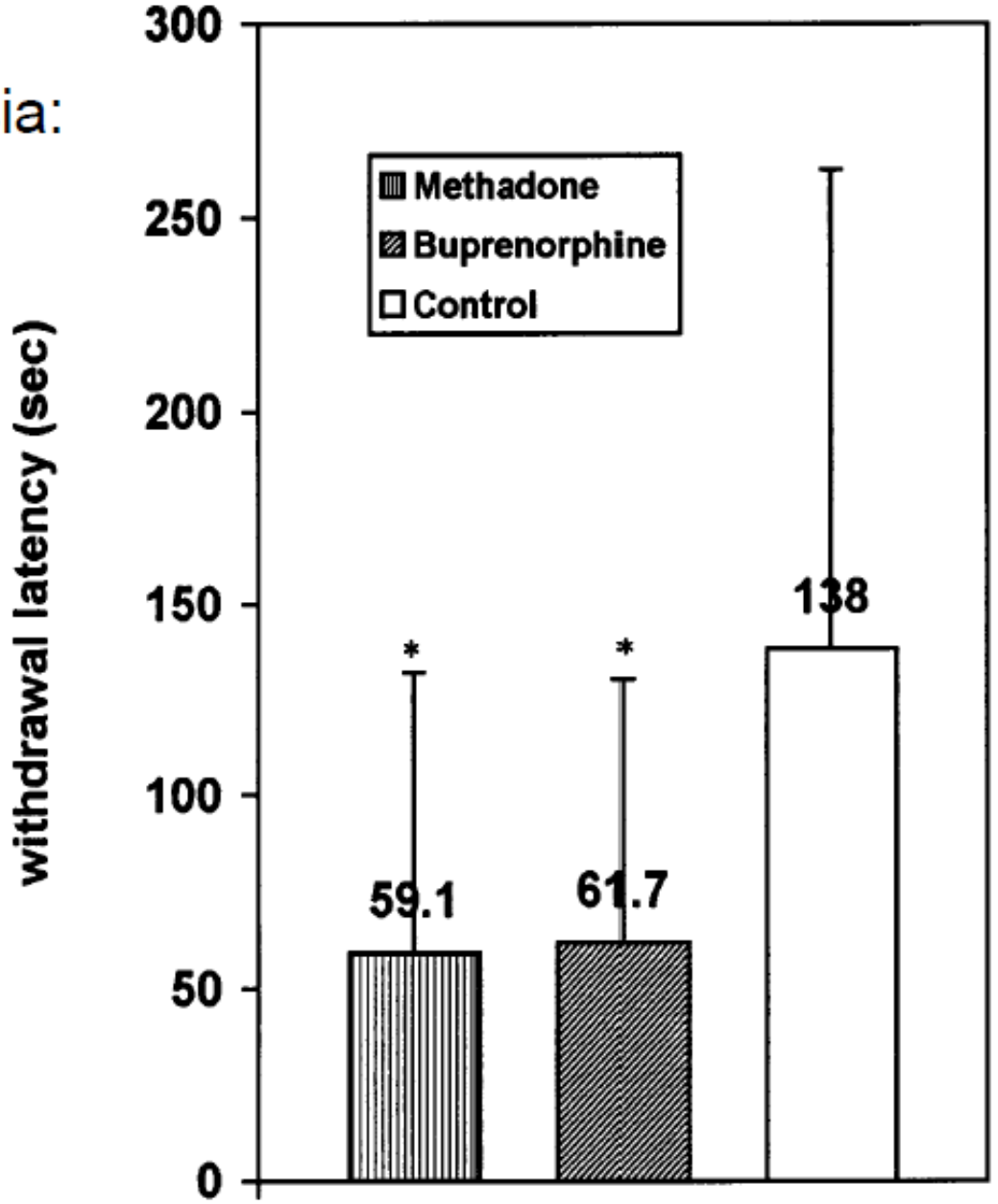
prevent withdrawal symptoms and allow counseling for the underlying disease

- Methadone: pure mu agonist with half life of 24 hours
- Buprenorphine: partial mu agonist, partial kappa antagonist, very tight binding to mu receptors with 24-36 hour half life. Ceiling effect at approx 32 mg qd.
- Both allow for daily administration in tightly regulated conditions
- FDA directs that only methadone treatment centers can treat opiate dependence with methadone
- Buprenorphine is approved for office based treatment (non-pregnant) of opioid dependence

Opioid induced hyperalgesia: A real phenomenon

Both methadone and buprenorphine demonstrated reduced pain tolerance to a standardized pain stimulus (hyperalgesia)

Cold-pressor withdrawal latency in long-acting opioid-maintained former opioid addicts and matched controls. Each bar (and bracket) represents the mean value (and SD) for the subjects derived from three testing sessions.



Compton, 2001

Summary of the clinical problem

- Opiates are among the most effective analgesics available
- Long term use can create pharmacodynamic tolerance and hyperalgesia
- Our patients maintained on long term opiates are undergoing a painful process
  - What do we know about labor, delivery, and post-operative pain in women maintained on methadone
  - What do we know about women maintained on buprenorphine
  - What alternative/adjunctive analgesic modalities might work

Common Analgesia questions: Women maintained on methadone versus buprenorphine

- Should women stop buprenorphine before delivery to improve pain control?
- Does regional analgesia work?
- How should post vaginal delivery pain be managed?
- How should post-op pain be managed?

Alford, Annals Int Med 2006

Common Analgesia questions: Women maintained on methadone versus buprenorphine

- Should women stop buprenorphine before delivery to improve pain control?
  - No: it will create the potential for term withdrawal, which we have tried to avoid through pregnancy
  - Reasonable to continue whatever medication for opioid dependence to avoid withdrawal
- Does regional analgesia work?
- How should post vaginal delivery pain be managed?
- How should post-op pain be managed?

Common Analgesia questions: Women maintained on methadone versus buprenorphine

- Should women stop buprenorphine before delivery to improve pain control?
- Does regional analgesia work?
  - Yes
- How should post vaginal delivery pain be managed?
- How should post-op pain be managed?

Alford, Annals Int Med 2006

Efficacy of neuraxial analgesia: similar

	Methadone N=36	Control N=35	p
Pain before NA	9 (8, 10)	9 (7.5, 10)	0.86
Pain after NA	1 (0, 3.3)	1.3 (0, 2)	0.77
PCEA settings			
Basal (cc/hr)	11.7± 1.7	10.6 ± 1.6	0.19
Delay	6.6 ± 1.9	6.1 ± 1.7	0.32
Bolus	8.0 ± 2.8	8.0 ± 2.5	0.96
1 hour max infusion	34.6 ± 1.6	34.0 ± 3.0	0.38
Extra bolus needed during labor	11 (30.6)	4 (11.4)	0.08

Efficacy of neuraxial analgesia: similar (maybe more epidural boluses)

	Buprenorphine N=46*	Control N=45*	p
Pain before NA	9 (8, 10) N=39	8.8 (8, 10) N=42	0.74
Pain after NA	2 (0, 3.6) N=34	2 (0, 4) N=41	0.29
PCEA settings* (Stand Sol: 1/16% bupivicaine+2 mcg fentanyl/cc)			
Basal (cc/hr)	10.2±0.6 n=46	10.1±0.7 n=42	0.60
Delay	7.8±2.6 N=46	9.5±1.5 n=42	0.007
Bolus	6.7±1.6 n=46	7.4±1.3 n=42	0.02
1 hour max infusion	35.7 ±1.8 N=46	35.8 ±1.2 N=41	0.90
Extra bolus needed during labor**	19/46 (30.6)	8/43 (11.4)	0.04

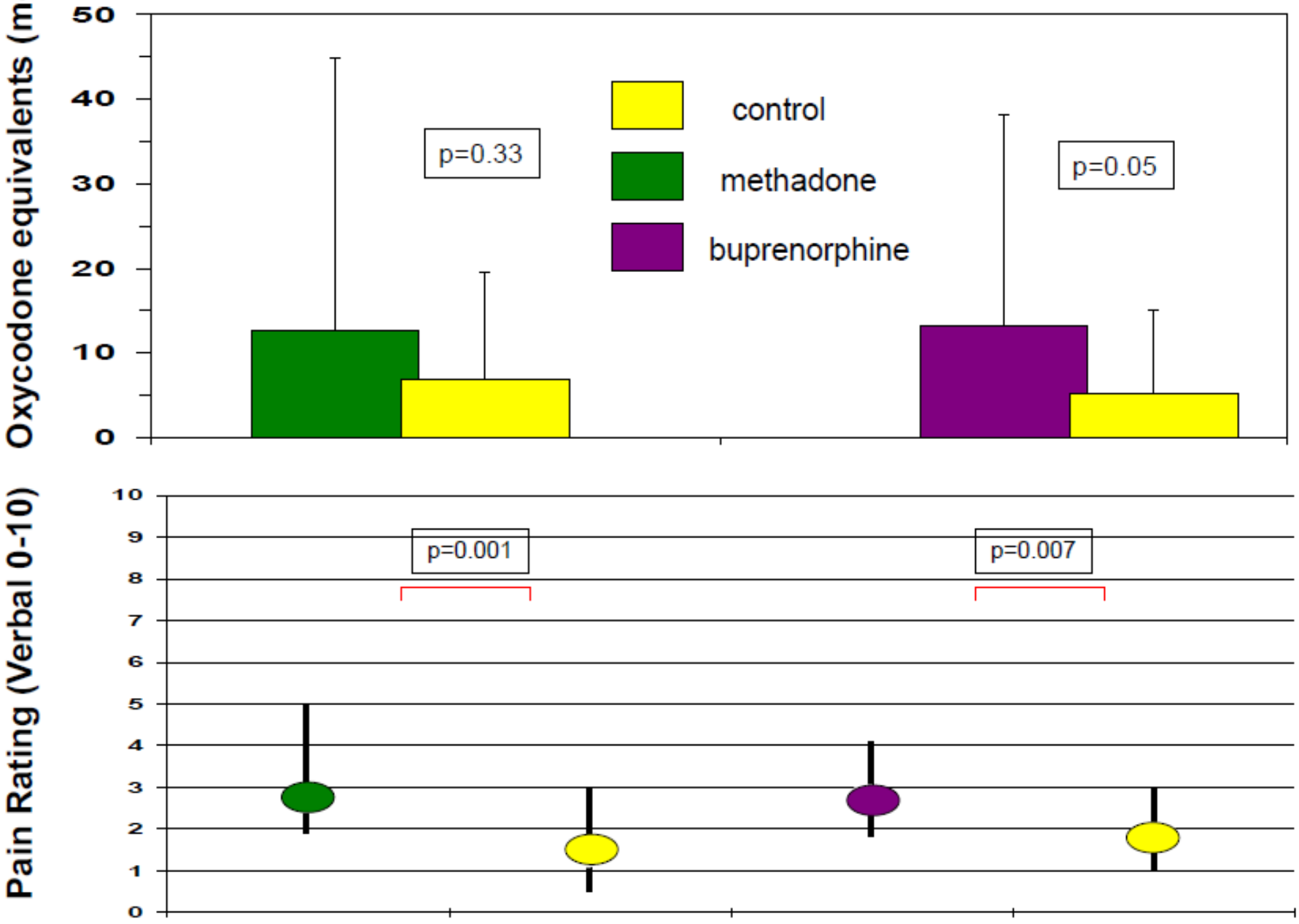
* Data omits: one case that had no relief from the epidural and it was felt to be in the wrong space; patient received spinal with good relief; two controls that received epidural but delivered prior to starting PCEA **not normalized to duration of epidural (yet)

Common Analgesia questions: Women maintained on methadone versus buprenorphine

- Should women stop buprenorphine before delivery to improve pain control?
- Does regional analgesia work?
- How should post vaginal delivery pain be managed?
  - Similar to other patients: access to short acting opioids
- How should post-op pain be managed?

Alford, Annals Int Med 2006

Postpartum vaginal delivery opioid use and pain score: 24 hrs PP: Women treated with methadone or buprenorphine have more pain



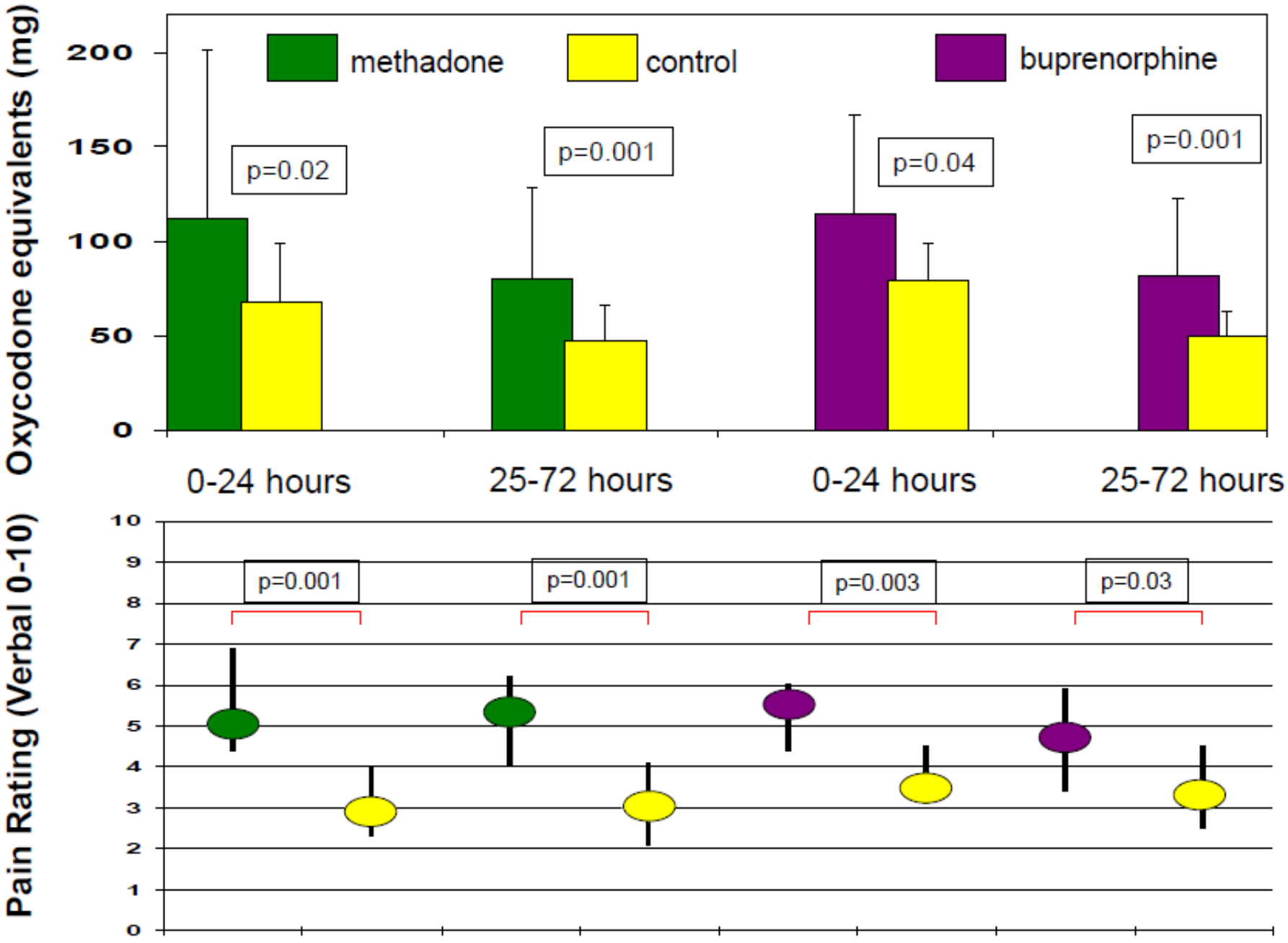
Meyer, Ob Gyn 2007; Euro J Pain 2010

Common Analgesia questions: Women maintained on methadone versus buprenorphine

- Should women stop buprenorphine before delivery to improve pain control?
- Does regional analgesia work?
- How should post vaginal delivery pain be managed?
- How should post-op pain be managed?
  - IV and short acting opioids
  - Consider split dose of maintenance medication
  - PCEA x 24 hrs if severe, intractable pain

Alford, Annals Int Med 2006

Postoperative cesarean delivery opioid use and pain score: 70% more opioid required



Meyer, Ob Gyn 2007; Meyer Euro J Pain 2010

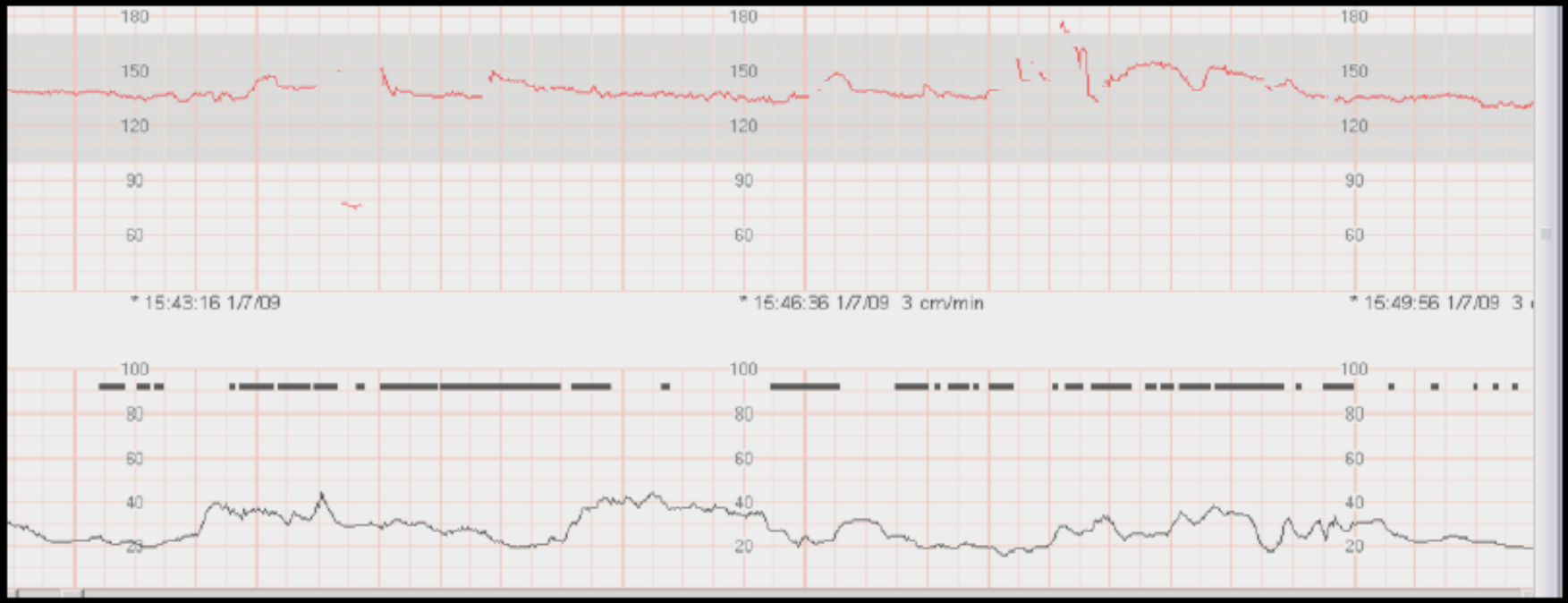
AVOID AGONSIT/ANTAGONISTS:

Nalbuphine

Butorphanol

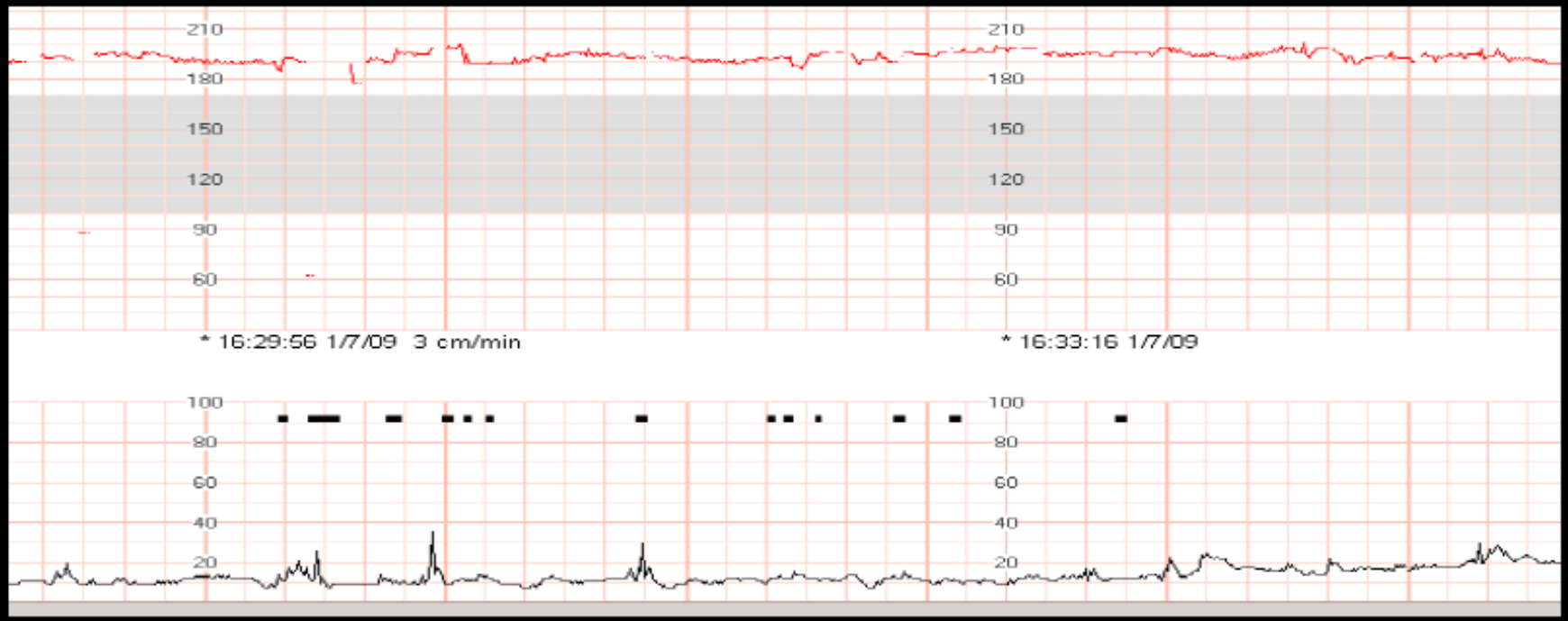
ALERT:
Nalbuphine and butorphanol are partial opioid agonists and can precipitate acute withdrawal in opioid dependent patients

Patient maintained on methadone requested medication for pain



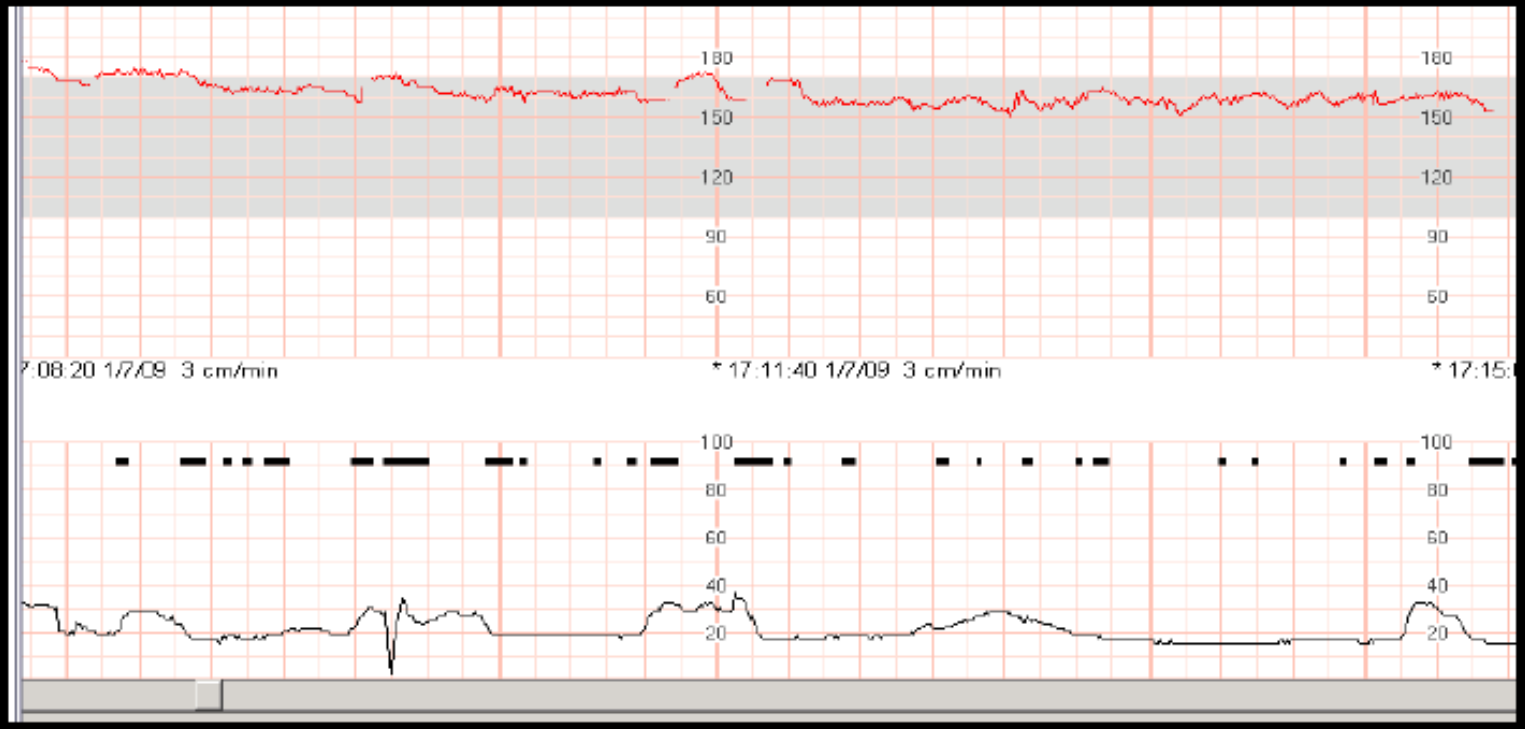
Received nalbuphine 10 mg IV

- Physical Exam
  - Agitated, crying, c/o severe abdominal cramps, muscle cramps- worse in legs, cold w/ shaking chills, tremulous
  - RR subjectively increased→no vitals recorded
  - Abd S/NT, fundus soft, ↑BS
- Fetal Tachycardia



Received IV morphine

- Fetal Tachycardia continued x 45min., with subsequent return to baseline
  - No decelerations



Comparison of Post-Cesarean Section Opioid Analgesic Requirements in Women With Opioid Use Disorder Treated With Methadone or Buprenorphine

Methadone postoperative: 97.7 mg±65.6 (morphine equivalents)
Buprenorphine 85.1 mg ± 73.0

There is no evidence that stopping buprenorphine helps with post-operative pain control.

Authors: Vilkins, Annmarie L.; Bagley, Sarah M.; Hahn, Kristen A.; Rojas-Miguez, Florencia; Wachman, Elisha M.; Saia, Kelley; Alford, Daniel P.
Source: Journal of Addiction Medicine, Volume 11, Number 5, September/October 2017, pp. 397-401(5)

To Stop or Not, That Is the Question

Acute Pain Management for the Patient on Chronic Buprenorphine

T. Anthony Anderson, Ph.D., M.D., Aurora N. A. Quaye, M.D., E. Nalan Ward, M.D., Timothy E. Wilens, M.D., Paul E. Hilliard, M.D., Chad M. Brummett, M.D.

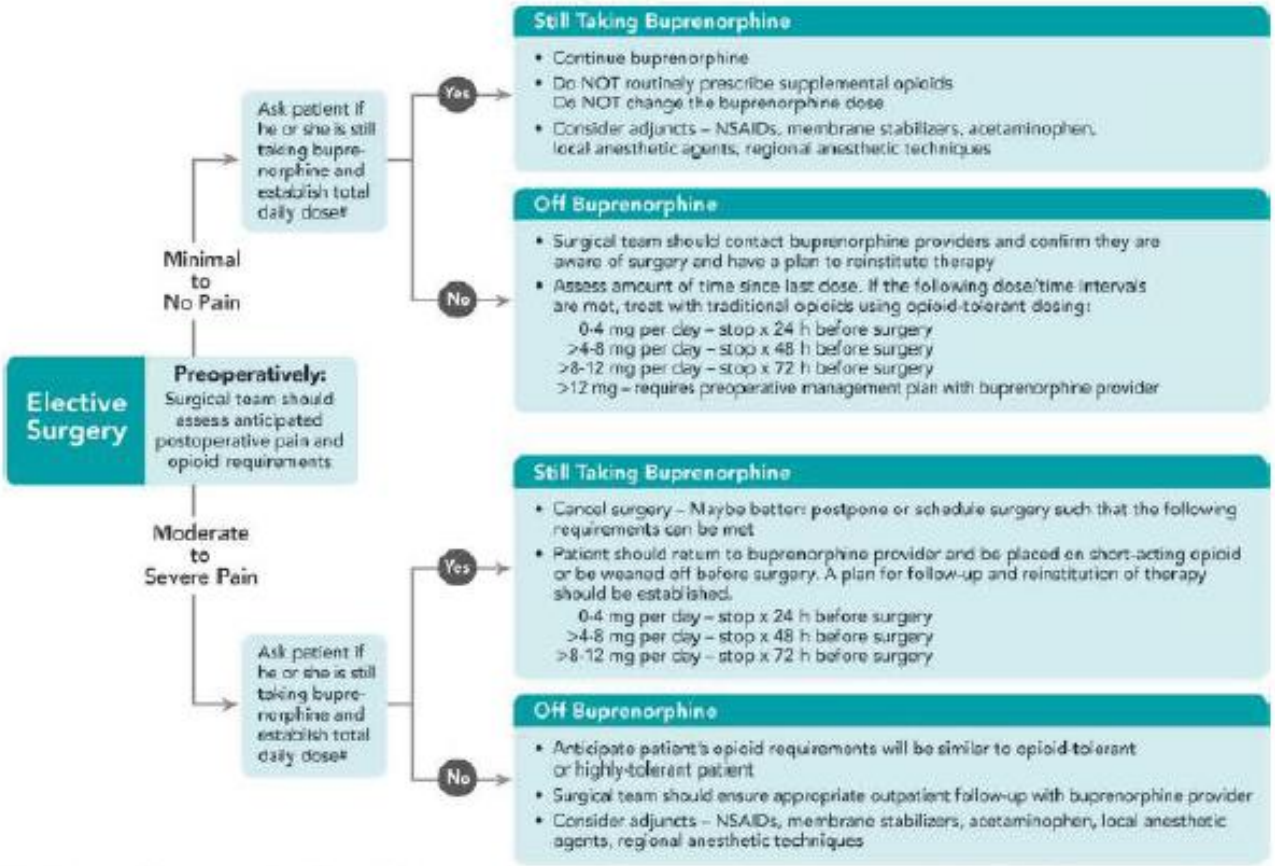
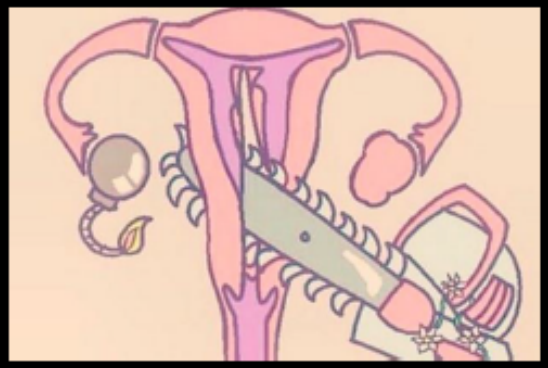


Fig. 1. Suggestions are outlined for patients presenting for elective surgeries taking buprenorphine. NSAIDs = nonsteroidal anti-inflammatory drugs. *Transdermal buprenorphine need not be discontinued prior to elective surgery regardless of dose.

Anesthesiology, V 126 • No 6
2017

Take home messages regarding postpartum and postoperative pain



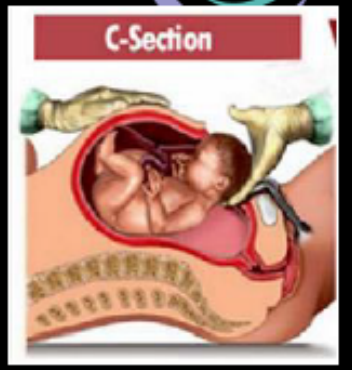
- Pain scores are higher in women on either methadone or buprenorphine compared to controls after both vaginal birth and cesarean delivery
- Women having a vaginal birth require modest amounts of opioid analgesics, not significantly different from control patients
- Women maintained on methadone or buprenorphine require about 50% more opioid analgesic postoperatively compared to control patients
- Intrathecal opioids do not appear to reduce the opioid requirements significantly and can cause itching
- A few patients may have intractable pain and require PCEA

Women with OUD and Controls both reduced opioid use by about 1/3 from POD 1 to POD 3.

We saw no evidence of drug seeking in labor or postpartum.

Admission:
Assess OUD treatment and MAT dose if applicable
Assess for withdrawal if untreated OUD
Obtain urine drug screen as indicated
Order MAT on schedule to avoid withdrawal

Patient requests pharmacologic pain relief:
Full opioid agonist (*contraindicated: nalbuphine, butorphanol*)
Neuraxial (epidural, spinal, combined)



Vaginal delivery

Standard dose:
Acetaminophen
NSAID
Opioids prn

Discharge:
Acetaminophen
NSAID
(Opioids prn for extensive lacerations)
Same MAT dose

Cesarean delivery

Consider Perioperative adjuncts:
Intrathecal opioid (caution due to pruritus)
Low dose ketamine
Gabapentin
TAP block
Infiltration of wound with local anesthetic
Parenteral ketorolac

Postoperative and Discharge:
NSAID
Acetaminophen
Opioids: increase opioid equivalents 50-70%: hydromorphone 2-4 mg q4-6 hrs (7 days total)
Same MAT dose

Adjunctive therapy:
modest effect in non-opioid population

International Journal of Obstetric Anesthesia (2011) 20, 3–9
0959-289X/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ijoa.2010.10.002

ORIGINAL ARTICLE

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Low-dose ketamine with multimodal postcesarean delivery analgesia: a randomized controlled trial

J.R. Bauchat, N. Higgins, K.G. Wojciechowski, R.J. McCarthy, P. Toledo, C.A. Wong
Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

N=85 (ketamine)/89 (saline)
No effect on pain control or medication use
Increased sedation

Randomized controlled trial of intravenous acetaminophen for postcesarean delivery pain control

Brie Altenau, MD; Catrina C. Crisp, MD, MSc; C. Ganga Devaiah, MS; Donna S. Lambers, MD

American Journal of Obstetrics & Gynecology SEPTEMBER 2017

30% reduction in oxycodone

TABLE 2
Comparison of breakthrough pain medications during inpatient stay

Pain medications	IV acetaminophen (n = 57)	Placebo (saline) (n = 47)	*P* value[a]
	Mean (SD)		
Total oxycodone, mg[b]	47.0 (39.1)	65.0 (46.2)	.034[c]
Total number of breakthrough Medications	19 (7)	21 (7)	.133
Total ibuprofen, mg	4786 (2333)	5260 (1915)	.267
	Median (IQR)		
Total morphine, mg	5.0 (5.0–5.0)	5.0 (5.0–5.0)	.168
Total fentanyl, mcg	100.0 (0.0–100.0)	100.0 (0.0–100.0)	.214
Total ketorolac, mg	30.0 (30.0–60.0)	30.0 (30.0–60.0)	.723
Total nalbuphine, mg	0.0 (0.0–20.0)	0.0 (0.0–10.0)[d]	.918

IQR, interquartile range.

[a] Computed using the Student *t* or Mann-Whitney *U* test. [b] Does not include amount of oxycodone in Percocet if patient received Percocet. [c] Statistically significant at the .05 alpha level. [d] Denotes 1 missing observation.

Altenau et al. RCT of IV acetaminophen for cesarean delivery. Am J Obstet Gynecol 2017.

Gabapentin Improves Postcesarean Delivery Pain Management: A Randomized, Placebo-Controlled Trial

Albert Moore, MD,* Joseph Costello, MD,* Paul Wieczorek, MD,* Vibhuti Shah, MD,†
Anna Taddio, PhD,§ and Jose C. A. Carvalho, MD, PhD*†

N=46 each group:
Pain score 24 hrs: 2.1 vs 4 (p<0.01)
No difference oxycodone
Increased sedation gabapentin

Anesth Analgesia 2011

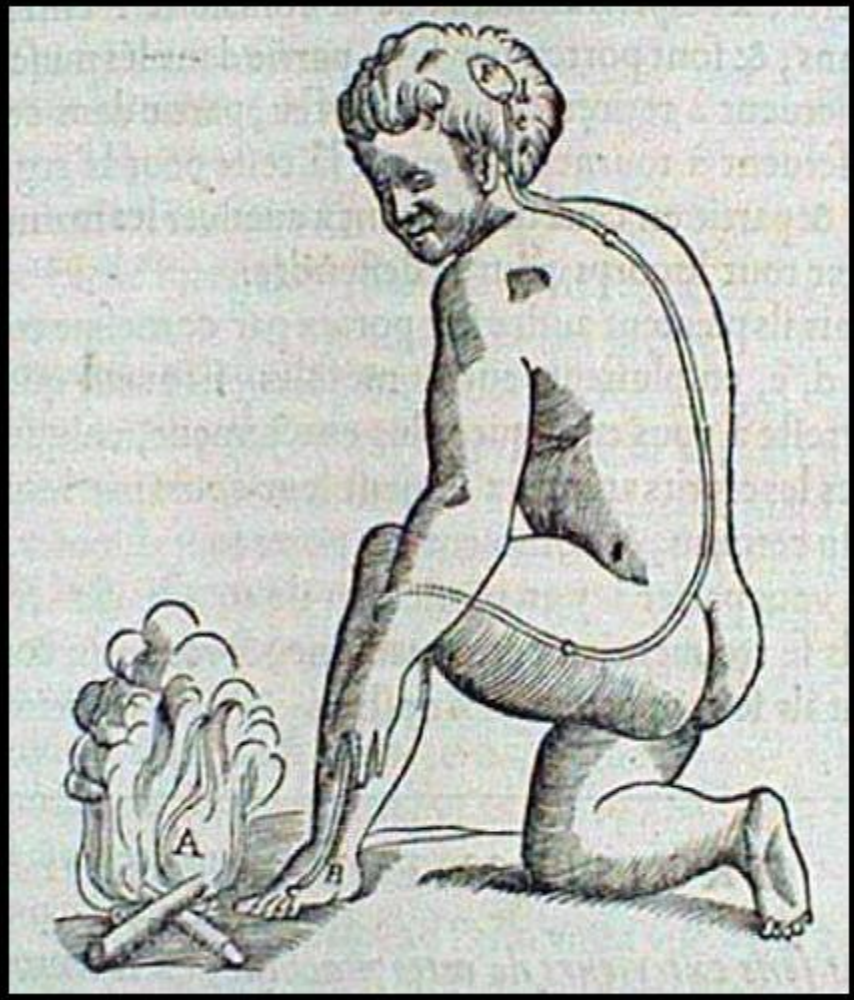
Pain is inextricably linked to action

I think, therefore I am….

- *Believed that only humans had minds; the body was mechanical, obeying the laws of physics; the mind was nonmaterial and acted through the body through the pineal gland.*

- *Not only does the mind control the body, but the body controls the mind (ie: actions performed out of passion)*

French philosopher Rene Descartes (1596-1650): the first mind-body practitioner



Questions?

This webinar was recorded and will be available to view within 5 days at vchipobstetrics.org

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UNIVERSITY OF VERMONT LARNER COLLEGE OF MEDICINE

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-**June 11, 2019 @ 12:15pm** Severe Maternal Morbidity & VT Dept. of Health Topic

To Register visit: vchipobstetrics.org

Contact: Amanda.slater@uvmhealth.org

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Thank you!