

Perioperative Care of the Opioid-Dependent Patient

M. Gabriel Hillegass, M.D.

Associate Professor of Anesthesiology & Perioperative Medicine

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32nd Annual Update in Psychiatry: Opioids & Pain Management



Disclosures

None



Learning Objectives

1. Identify KEY STEPS in the perioperative evaluation of patients on chronic opioid therapy & in the implementation of an analgesic treatment plan.
2. Highlight clinical pearls and appreciate the complexities for the perioperative management of opioids used in addiction medicine.





Relevance of Optimal Pain Management

- Pain as 5th Vital Sign
- Institute of Medicine Report
- The Guideline(s)
- Value-Based Healthcare
- Perioperative Surgical Home

Why an Opioid Overdose Epidemic?

- Opioids are effective for acute pain and palliation at end-of-life
 - › But they have limited effectiveness long-term with increased risk!
- Relatively cheap medications
- Typically covered by insurance
- Societal, ethical, moral, and legal expectations to treat severe pain with strong pain medication
- Pharmaceutical pressure on providers and patients
- Inadequate training of health care professionals has led to lack of critical appraisal of risks and insufficient knowledge of appropriate mitigation strategies
 - › Also lack of understanding of alternative treatment algorithms



“Pain as the 5th Vital Sign”

- In 1995, the **American Pain Society** promulgated that the 1st step in improving pain care is to assess and document patients' report of pain
 - › APS presidential address (Nov 1996), “... vital signs are taken seriously... if pain were assessed with the same zeal as vital signs, it would have a much better chance of being treated properly.” —James Campbell, MD
- In 1999, “Pain as the 5th Vital Sign” initiative launched by the **Veterans Health Administration** to improve pain management
 - › Required pain intensity rating (NRS 0-10) at all clinical encounters
 - › Expected pain scores of 4 or more would trigger a comprehensive pain assessment and prompt intervention





May 22, 2019

Dear American Pain Society Members:

It is with heavy hearts that we write to inform you that it is the recommendation of the Board of Directors that American Pain Society (APS) cease its business operations.

As many of you may recall from the communications you received from President Bill Maixner over the past six months, APS has been named as a defendant in numerous spurious lawsuits and is subject to numerous subpoenas. Despite our best efforts, APS was unsuccessful in its attempts to resolve these lawsuits without the need for what will no doubt be lengthy and expensive litigation. The anticipated time-consuming and costly litigation combined with the declining membership and meeting attendance has created the perfect storm placing APS in a precarious financial position. Constrained by these unfortunate circumstances, we do not believe APS can continue to fulfill its mission and meet the needs and expectations of our members and community.

After significant consideration, including painstaking legal review and lengthy Board discussions and examination of alternative scenarios that would allow APS to continue, it is the recommendation of the APS Board of Directors (11 for and 1 against) that the membership vote in favor of filing a voluntary petition under Chapter 7 of the Bankruptcy Code. Chapter 7 is a process whereby an independent third party trustee is appointed under bankruptcy court supervision to take possession of the assets of APS and administer those assets for the benefit of the creditors of APS. Importantly, upon the filing of a Chapter 7 bankruptcy case, all lawsuits pending against APS will be subject to an automatic stay pending further order of the bankruptcy court. This will allow APS to minimize legal expenses and maximize recoveries for its creditors, as opposed to future dissipation of assets in defending the lawsuits which have no end in sight.

In order to proceed with a chapter 7 filing, at least 10% of our eligible membership must vote, with the majority of these votes approving the filing of a Chapter 7 bankruptcy case and the proposed Resolution in the attached ballot. APS currently has 1,173 voting members, and therefore, at least 117 must vote.

So many of you have dedicated your time, energy, passion, and expertise to building and sustaining this organization - from founders who continue to be members to early-career professionals who have committed to the field of pain science and served the Society dutifully. Many of us have grown our professional careers through our interactions and participation with APS. We are truly thankful for all the contributions and efforts made by the members of APS (past and present) to further the mission of APS.

Your vote to approve the Resolution (which follows the recommendation of the Board) does not in any way signify that you are happy about bringing APS to the conclusion of its current life cycle. The Board does not make its recommendation lightly, but believes a Chapter 7 case, under the circumstances, is the most appropriate and responsible manner to complete this chapter of APS and the good work it has done.

In order for your vote to be counted, we must receive it by 11:55 p.m. CDT on Wednesday, May 29th so that we may advance the process and mitigate further legal risk to APS.

Thank you,
The APS Board of Directors

Measuring Pain as the 5th Vital Sign Does Not Improve Quality of Pain Management

Richard A. Mularski, MD, MSHS,^{1,2} Foy White-Chu, MD,³ Deborah Overbay, MS, RN,⁴ Lois Miller, PhD, RN,⁴ Steven M. Asch, MD, MPH,^{1,2} Linda Ganzini, MD, MPH^{5,6}

¹VA Greater Los Angeles Healthcare System, Department of Medicine, Los Angeles, CA, USA; ²The University of California, Los Angeles and RAND Health, Los Angeles, CA, USA; ³Department of Medicine, Oregon Health & Science University, Portland, OR, USA; ⁴School of Nursing, Oregon Health & Science University, Portland, OR, USA; ⁵Department of Psychiatry, Oregon Health & Science University, Portland, OR, USA; ⁶Portland Veterans Affairs Medical Center, Mental Health Division, Portland, OR, USA.

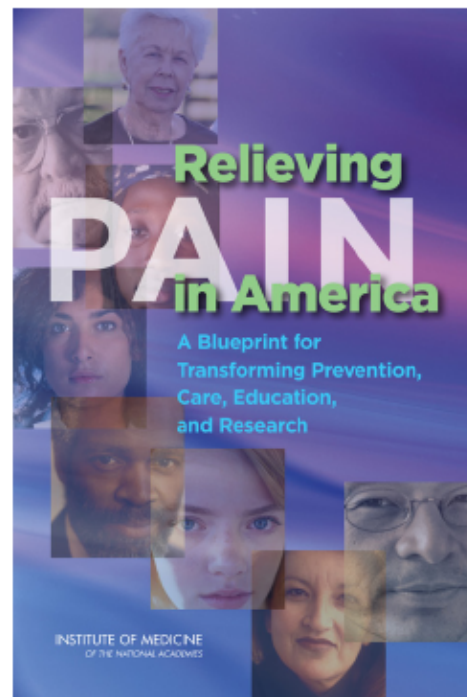
- Retrospective review of the VA's 5th vital sign initiative
 - › Examined 7 process indicators of quality pain management
 - › 300 randomly selected visits before & 300 visits after initiative in a primary care general medicine outpatient clinic
 - › Of the patient's w/ substantial pain (NRS of 4 or more):
 - › 22% had no attention to pain documented in EMR
 - › 27% had no further assessment documented
 - › 52% received no new therapy for pain at that visit
- Quality of pain care was unchanged
- Patients w/ documented significant pain often had inadequate pain management



For more information visit www.iom.edu/relievingpain

Relieving Pain in America

A Blueprint for Transforming Prevention, Care, Education, and Research



Report initiated through HHS as a requirement of the *2010 Patient Protection and Affordable Care Act (PPACA)*



IOM's Relieving Pain in America Report

“A cultural transformation is necessary to better prevent, assess, treat & understand pain of all types.”

- › Increase awareness about pain & its health consequences
- › Emphasize *prevention* of pain
- › Improve *pain assessment & management* in the delivery of health care
- › *Encourage self-efficacy* using public health communication strategies to inform patients on how to self manage pain
- › Tailor pain care *to each patient's experience*
- › *Address disparities* in the experience of pain among subgroups of the population

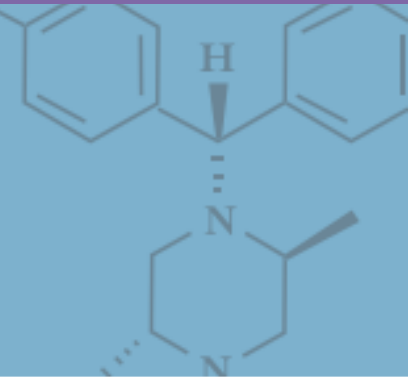




U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN



IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC's *Guideline for Prescribing Opioids for Chronic Pain* is intended to improve communication between providers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder and overdose. The Guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.



VA/DoD Guidelines (February 2017)



VA/DoD CLINICAL PRACTICE GUIDELINE FOR OPIOID THERAPY FOR CHRONIC PAIN

Department of Veterans Affairs

Department of Defense



Common Guideline Principles

- Non-opioid therapy is preferred for chronic pain
 - › PT, exercise, CBT, multimodal analgesics, interventional treatments = comprehensive/interdisciplinary care is key
- Use lowest possible opioid dose
- Initiate with short-acting opioid formulations
- Always use good judgement and risk mitigation strategies
- Obtain informed consent (discuss risks & benefits)
- Establish goals for pain, function and QoL
- Monitor, monitor, monitor for misuse, abuse, diversion and other adverse outcomes



Pain Management and the Opioid Epidemic

**Balancing Societal and Individual Benefits and Risks of
Prescription Opioid Use**

**Report Release
July 13, 2017**

**Board on Health Sciences Policy
Health and Medicine Division**

Addressing the Opioid Epidemic

- Restrict the lawful supply
 - › Drug take-back programs
- Influence prescribing practices
 - › Provider education (national evidence-based approach)
 - › Prescription drug monitoring programs
 - › Insurance-based approaches
- Reduce demand
 - › Patient (and provider) education
 - › Medication-assisted treatment for OUD
- Reduce harm
 - › Naloxone



“Not Allowed to Be Compassionate”

Chronic Pain, the Overdose Crisis, and Unintended Harms in the US

- Involuntary tapering of opioids is a violation of human rights
- Healthcare providers are turning away patients on chronic opioid therapy
- Insurance companies and programs are refusing coverage
- State governments are *preventing physicians from using their medical judgement* to provide appropriate care

*Misinterpretation of the 2016 CDC Guideline on Opioid Prescribing being used to justify these actions

Human Rights Watch

“Not Allowed to be Compassionate”

- Recommendations to federal and state governments:
 - Limit the unintended consequences of the response to the overdose crisis for chronic pain patients;
 - Ensure continuity of care for patients of shuttered pain clinics;
 - Improve availability, accessibility and affordability of multimodal pain management, including non-pharmacological modalities; and
 - Improve data collection on the overdose crisis



CDC Response to Human Rights Watch

- The Guideline is a set of *voluntary* recommendations to guide primary care providers as they work in consultation with their patients and specialists to address chronic pain
- The Guideline encourages physicians to use their clinical judgement and base treatment on what they know about their patients, including initiation and maintenance of opioids when benefits > risks
- Regarding determination of opioid dosage limitation recommendations:
 - 50-99 MME/day – increase OD risk *2-5x* compared to 1-19 MME/day
 - >100 MME/day – increase OD risk *up to 9-10x* 1-19 MME/day risk
- Involuntary tapering is not recommended by the CDC
 - Tapering should be done with patient buy-in when risks > benefits



Value-Based Health Care

Hospital Value-Based Purchasing Program

- › Another initiative from the PPACA of 2010
 - › Rewards QUALITY rather than quantity of health care
 - › “Fee-for-value” versus “fee-for-service”
 - › Multiple quality measures exist & are still being defined & validated across the medical disciplines
 - › Patient experience in the hospital is one such measure
- VALUE = OUTCOMES / COSTS**
- › Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey
 - › 27 questions related to hospital experience given at discharge
 - › As of FY2013, CMS is linking 1-2% of payments for how well hospitals perform on HCAHPS



Value-Based Health Care

✦ HCAHPS, continued

○ Major response categories include:

- › Communication with health care providers
- › Responsiveness of hospital staff
- › Cleanliness & quietness of the hospital environment
- › **Pain management**

○ Specific questions regarding pain management include:

1. Did you need medicine for pain?
2. How often was your pain well controlled?
3. How often did the hospital staff do everything they could to help you with your pain?

- Do you foresee any challenges with respect to caring for patients on chronic opioid therapy or medication assisted treatment?



Does patient perception of pain control affect patient satisfaction across surgical units in a tertiary teaching hospital?

Hanna MN¹, González-Fernández M, Barrett AD, Williams KA, Pronovost P.

⊕ Author information

Abstract

In this study, the relationship between patients' perceptions of pain control during hospitalization and their overall satisfaction with care was examined. Satisfaction data were collected from the federally mandated Hospital Consumer Assessment of Healthcare Providers and Systems survey for 4349 adult patients admitted to any surgical unit over an 18-month period. Patients' perceptions of pain control and staff's efforts to control pain were associated with their overall satisfaction scores. These perceptions varied widely among services and nursing units. Interestingly, patient satisfaction was more strongly correlated with the perception that caregivers did everything they could to control pain than with pain actually being well controlled. The odds of a patient being satisfied were 4.86 times greater if pain was controlled and 9.92 times greater if the staff performance was appropriate. Hospitals may improve their patients' satisfaction by focusing on improving the culture of pain management.

Patient satisfaction was strongly correlated w/ *perception that everything possible has been done to control pain* rather than actual pain control.

- › Communication, bedside manner, courtesy & empathy are paramount
- › **Expectation management** should begin with the surgeon and Pre-Operative Clinic & continue in the holding area on the day of surgery
- › Early involvement of expert resources such as the Regional Acute Pain Service



Perioperative Surgical Home

New practice model to address the current disjointed & costly perioperative system

- › Current system weaknesses:

- › Poor coordination of care; inconsistent care from both surgery & anesthesiology; **volume-driven; not patient-centered**
- › Discrete episodes of care include preop, intraop, postop, post-discharge w/ different medical providers & poor communication throughout

The PSH model aims to **reduce variability** & emphasizes patient-centeredness *by treating the entire perioperative period as one continuum of care* (from decision to operate to 30 days post-op)

- › Shared decision-making by both surgery & anesthesiology
- › Creation of clear, evidence-based algorithms of care based on acuity, comorbidities & risk factors
- › Anesthesiology-led clinical management across specialty lines
- › Measures & seeks to improve clinical outcomes & cost-efficiency



Improving Perioperative Outcomes – Challenges & Solutions



- Pain Chronification
- Complexity of Chronic Pain
- ERAS & Multimodal Protocols
- PROSPECT
- Michigan-OPEN

Pain Chronification

- Process by which transient (acute) pain transitions into chronic pain
 - **Acute pain** = normal, predicted **physiological** response to a noxious stimulus
 - **Chronic pain** = pain without biological value that persists beyond the normal tissue healing; usually beyond 3 months
 - → **PATHOLOGICAL STATE!** (no protective value)
- Changes in CNS pain processing due to an *imbalance* of pain amplification and pain inhibition
- Multiple factors determine the risk, degree & time-course
 - Genetic
 - Environmental
 - Biopsychosocial



Pain Chronification 2.0 – Pain Physiology

- For both nociceptive & neuropathic pain, ascending pathways transmit pain signals via neurons along the spinal cord and brainstem to the brain for interpretation
 - Glutamate is the predominant excitatory neurotransmitter
 - Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter
- Normally, there is a robust descending inhibitory tone
 - Modifies pain perception via the **noradrenergic** pain regulation system
 - Norepinephrine and serotonin are key neurotransmitters
- An *imbalance* between **amplified ascending pain signals & inadequate activation of descending inhibitory pathways** leads to chronic pain



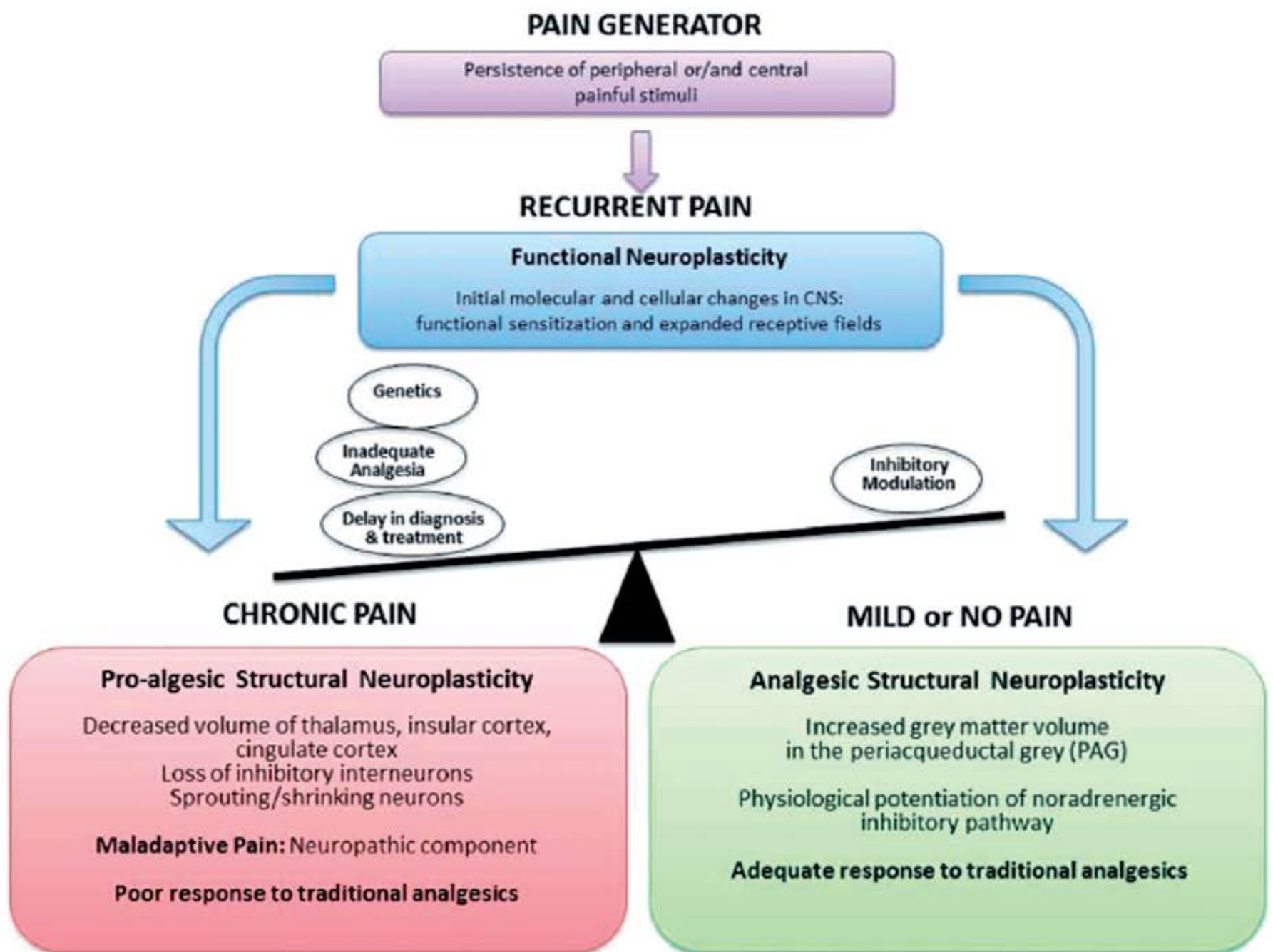


Figure 1. From the physiological perspective, an imbalance between enhanced ascending nociceptive inputs and inadequate inhibitory descending pathways is responsible for pain chronification⁴⁵. Reproduced with permission from Coluzzi *et al.*⁴⁵.

Pain Chronification 2.0 – Psychosocial Aspects

- Chronic pain *shifts brain representation* from nociceptive areas to emotional learning circuits
 - Likely leads to psychosocial features of chronic pain
- Chronic overlapping pain conditions (COPCs)
 - *Recent recognition that many common pain conditions have a high degree of coprevalence
 - Psychosocial factors play a key role
 - Complex interplay of multiple factors alters the balance between vulnerability and resilience to pain



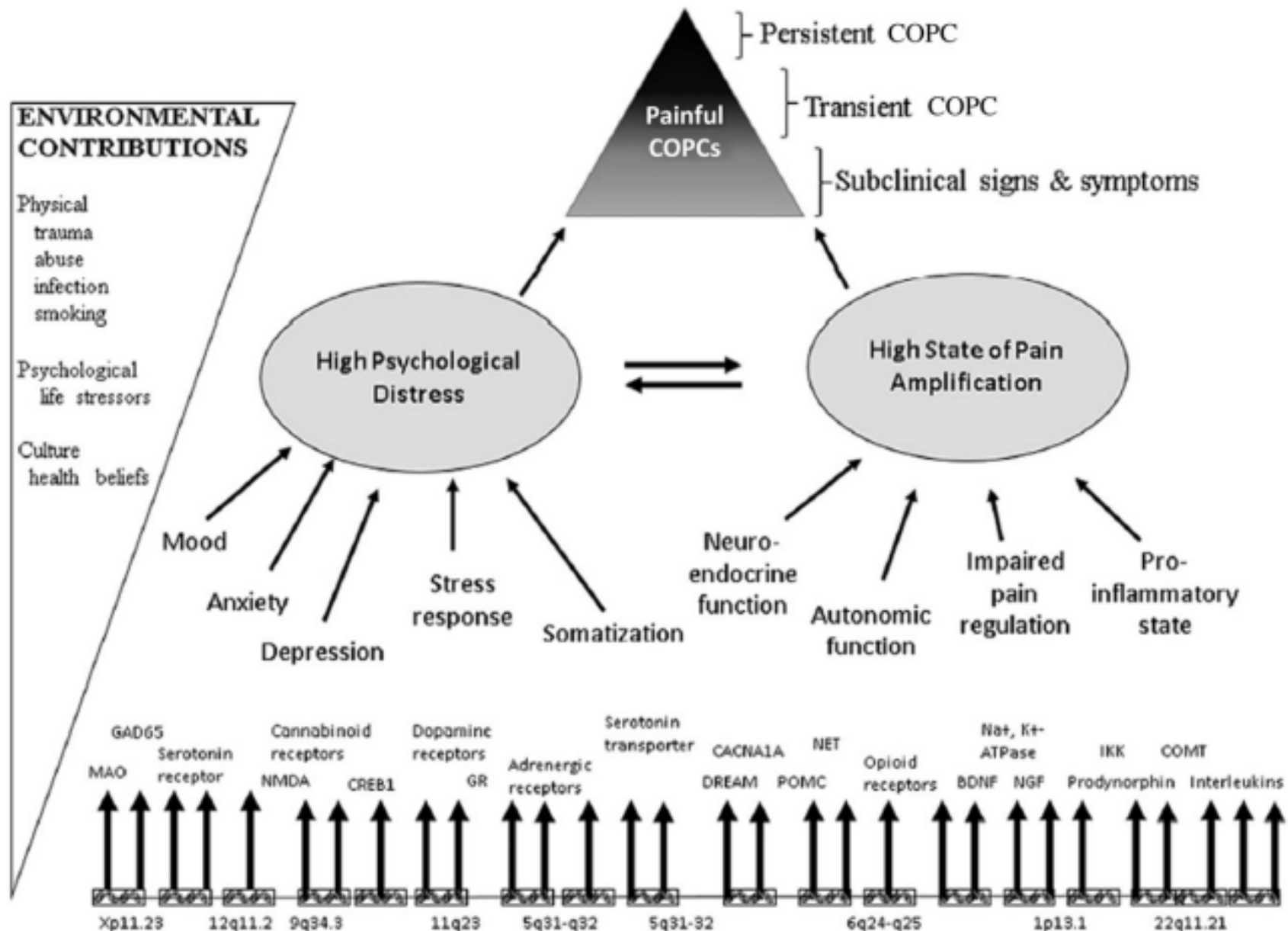


Figure 2. This model depicts likely determinants that contribute to the risk of onset and maintenance of common chronic overlapping pain conditions (COPCs). These factors are determined by genetic variability and environmental events that determine an individual's psychological profile and pain amplification status. These two primary domains are interactive and influence the risk of pain onset and persistence. Likely modifiers of the interaction between genetic and environmental factors include sex and ethnicity⁷². Abbreviations. MAO, monoamine oxidase; GAD65, glutamate decarboxylase; NMDA, N-methyl-D-aspartic acid; CREB1, CAMP responsive element binding protein 1; GR, glucocorticoid receptor; CACNA1A, calcium voltage-gated channel subunit alpha1A; POMC, proopiomelanocortin; NET, norepinephrine transporter; BDNF, brain-derived neurotrophic factor; NGF, nerve growth factor; IKK, IκB kinase; COMT, catechol-O-methyl transferase.

The Complexity of the Chronic Pain Patient

Disclaimer: These traits do not apply to all patients suffering from chronic pain conditions!

- Comorbid mental health illness, such as anxiety, depression, PTSD, etc.
- Poor/immature/maladaptive coping skills
- Other psychosocial barriers to self efficacy
- Opioid tolerance, dependence, hyperalgesia
- POLYPHARMACY
 - › Drug interactions
 - › Varying dosing schedules of analgesics in periop period
 - › Oral route of administration for most adjuvant agents



Polypharmacy in the Pain Patient

- NSAIDs
- Antidepressants & Anxiolytics
 - › TCAs
 - › SNRIs
 - › SSRIs
 - › MAOIs (rare)
- Antipsychotics
- Antiepileptics (AEDs)
- Benzodiazepines
- Hypnotics & other sleep aids (herbals common)
- Alpha-2 agonists
- Corticosteroids & other immunomodulators
- Topical creams & patches



Changes in Opioid Effects with Time

Loss of efficacy occurs w/ both short- & long-term opioid therapy

- › **Desensitization** – occurs w/ acute agonist use over min-hr, typically resolves in parallel w/ clearance of agonist
 - › MOA: 1) Phosphorylation of receptor & resultant uncoupling from G-protein; 2) Internalization of receptor via endocytic pathways
- › **Tolerance** – occurs w/ sustained agonist use over days-weeks, resolves over weeks w/ cessation of opioid use
 - › Reduction of maximal achievable effect → overcome w/ INC dose!
 - › Variable rates of onset of physiologic response tolerance:
 - › Pupillary miosis (little or no tolerance develops)
 - › Constipation (mild tolerance)
 - › Emesis, analgesia, sedation (moderate tolerance)
 - › Euphoria (rapid tolerance)



Changes in Opioid Effects with Time

- › **Cross-tolerance** – opioid agonists of same class will show reduced physiologic response in an organ system already rendered tolerant by another agent in that class
- › Incomplete cross-tolerance – reflects opioid receptor phenotypic variability and resultant inconsistency of the degree of cross-tolerance for a particular response
- › **Dependence** – state of adaptation in which a receptor/drug withdrawal response is produced by cessation of drug exposure
 - › **Withdrawal** = exaggerated physiologic responses d/t cellular activation in the CNS, adrenals & GI tract
 - › Increased somatomotor and autonomic outflow
 - › Agitation, hyperalgesia, hyperthermia, HTN, diarrhea, mydriasis, release of pituitary and adrenomedullary hormones
 - › Affective symptoms (dysphoria, anxiety, depression)



Changes in Opioid Effects with Time

- › **Addiction** – behavioral pattern characterized by compulsive use of a drug and continuous seeking of the drug despite negative impacts to the individual and to society
 - › Note: drug dependence does NOT equate to addiction!
 - › Tolerance and dependence are physiologic responses experienced in all patients and do not predict addiction
- › **Hyperalgesia** – “system level counter-adaptation”
 - › Enhanced excitability/activation of bulbospinal pathways that INC spinal dorsal horn transmission, thus INC pain response
 - › Chronic opioid receptor occupancy also activates PKC ultimately causing activation of local NMDA glutamate receptors
 - › This NMDA receptor activity causes INC spinal pain processing
 - › Blockade of NMDA receptors (e.g., ketamine) partially attenuates this loss of analgesic efficacy



Guidelines on the Management of Postoperative Pain

Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council

- Developed by multidisciplinary panel of experts
- Based on a systematic review of the evidence on postoperative pain management
- Numerous research gaps identified... only 4 of 32 recommendations were supported by high-quality evidence!

Guideline Recommendations

Categories:

- Preoperative education
- Perioperative pain management planning
- Use of different pharmacological and nonpharmacological modalities
- Organizational policies
- Transition to outpatient care

“Optimal pain management begins in the preoperative period with patient assessment and development of a plan that is tailored to the individual and surgical procedure involved.”



Setting Expectations

Ideally, a pain management plan is discussed during the preop visit, but taking the time in OR holding area should suffice

- › Address the patient's concerns & previous perioperative pain management experiences; carefully reconcile all opioids & adjuvant analgesics
- › Practice courtesy & empathy balanced w/ expert opinion to develop rapport
- › Outline potential perioperative treatment plan
- › Establish expectations for the patient, their family & surgical team
- › Educate the patient & their support network throughout the continuum
- › Adjust the pain management plan as needed; ongoing assessments are critical

Chou et al. Guidelines on the management of postoperative pain. J Pain. 2016;17:131-157.

Hadi et al. Brief review: perioperative management of the patient with chronic non-cancer pain. Can J Anes 2006;53:1190-99.



Coordination of Care

Coordinate care with other physicians/providers

- › Surgeon, PCM, Pain Physician, Psychiatrist, etc.
- › Consider bedside CAM approaches if available
- › Emotional support & spiritual counseling may be beneficial
- › Implement discharge analgesic plan & facilitate close follow up visit

Chou et al. Guidelines on the management of postoperative pain. J Pain. 2016;17:131-157.

Hadi et al. Brief review: perioperative management of the patient with chronic non-cancer pain. Can J Anes 2006;53:1190-99.



Enhanced Recovery After Surgery (ERAS)

- Concept developed in late 1990s by colorectal surgeon Dr. Henrik Kehlet (Denmark)
- ERAS protocols combine multiple scientific validated perioperative interventions into a synergistic package
 - Improvements in patient recovery
 - Enhanced patient safety
- Elements of ERAS:
 - Preoperative – education, medical optimization, prehabilitation
 - Intraoperative – multimodal analgesia, normothermia, SSI/DVT bundles
 - Postoperative – early nutrition, early mobilization, multimodal analgesia



Enhanced Recovery After Surgery (ERAS)

ERAS and Pain Management

- Multimodal approach seeks to reduce or eliminate (if possible) opioid medication
- Combination of two or more non-opioid analgesics or techniques
 - Regional anesthesia (central and/or peripheral blockade)
 - NSAIDs, AEDs, alpha-2 agonists, magnesium, ketamine, lidocaine, steroids, etc.
- Benefits include:
 - Reduced pain scores
 - Reduced opioid consumption
 - Reduced opioid-related adverse effects



Table 3. Options for Components of Multimodal Therapy for Commonly Performed Surgeries

Type of Surgery	Systemic Pharmacologic Therapy	Local, Intra-articular or Topical Techniques*	Regional Anesthetic Techniques*	Neuraxial Anesthetic Techniques*	Nonpharmacologic Therapies†
Thoracotomy	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶		Paravertebral block	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Open laparotomy	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶ i.v. lidocaine	Local anesthetic at incision i.v. lidocaine infusion	Transversus abdominis plane block	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Total hip replacement	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶	Intra-articular local anesthetic and/or opioid	Site-specific regional anesthetic technique with local anesthetic	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Total knee replacement	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶	Intra-articular local anesthetic and/or opioid	Site-specific regional anesthetic technique with local anesthetic	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Spinal fusion	Opioids‡ Acetaminophen‡ Gabapentin or pregabalin§ i.v. ketamine¶	Local anesthetic at incision		Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Cesarean section	Opioids‡ NSAIDs§ and/or acetaminophen	Local anesthetic at incision	Transversus abdominal plane block	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
CABG	Opioids‡ Acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶				Cognitive modalities TENS

Abbreviation: CABG, coronary artery bypass grafting.

NOTE. Blank cells indicate techniques generally not used for the procedure in question.

*Intra-articular, peripheral regional, and neuraxial techniques typically not used together.

†Use as adjunctive treatments.

‡Use i.v. PCA when parenteral route needed for more than a few hours and patients have adequate cognitive function to understand the device and safety limitations.

§May be administered preoperatively.

¶On the basis of panel consensus, primarily consider for use in opioid-tolerant or otherwise complex patients.



Regional Rules!

Consult Regional Anesthesia / Acute Pain Service

- › Ensure RAPS team is aware ASAP of potential need for a regional anesthetic and/or medical management postop
- › Regional techniques, both **peripheral** (single-shot or continuous) & **neuraxial** (SAB, PCEA, continuous EPA plus IV PCA), should be *strongly considered*
- › Patients still require at least 50% of baseline opioid dose to prevent withdrawal

Neuraxial opioids plus local anesthetic helpful in patients w/ significant opioid tolerance

- › IV:intrathecal conversion approximately 100:1
- › IV:epidural conversion approximately 10:1



Multimodal Perioperative Analgesia

- Maintain baseline opioid consumption
 - › If AM opioids not taken, load w/ equianalgesic dose
- Management of intrathecal drug delivery systems
 - › Continue intrathecal pain pump unchanged
 - › Consider decreasing baclofen pump dose preop (not required)
- Consider instituting **adjuvant analgesics** at any appropriate point along the perioperative continuum of care
 - › Schedule APAP, NSAIDs, AEDs, alpha-2 agonists, etc.
 - › Consider ketamine +/- dexmedetomidine infusions
 - › Avoid mixed agonists/antagonists d/t risk of withdrawal



Multimodal Perioperative Analgesia

- Intraoperatively, lipophilic opioids (e.g. fentanyl) preferred
 - › Dosing often 25-100% higher than opioid-naïve patients
 - › Calculate baseline hourly opioid use & INC intraop dose accordingly
 - › Alternatively, titrate opioid dose to RR after NMB reversal (at end of case)
- Postoperatively, IV PCA advantageous for convenience to patient, nursing & medical staff
 - › Most effective after an adequate loading dose has been given
 - › Appropriate dosing & frequent assessment required for efficacy
 - › Consider basal infusion rate of 50-100% of baseline opioid requirement
 - › Demand (bolus) dose of 25-150% of basal rate w/ appropriate lockout interval
 - › Studies have shown **higher patient satisfaction w/ PCA use** (when dosed appropriately)



Intraoperative methadone: Rediscovery, reappraisal, and reinvigoration?

Evan D. Kharasch, MD PhD

Division of Clinical and Translational Research, Department of Anesthesiology, and the Department of Biochemistry and Molecular Biophysics, Washington University in St. Louis, St. Louis, MO 63110

Methadone = opioid agonist & NMDA antagonist*

- › *Useful for opioid tolerance and hyperalgesia
- › Opioid w/ longest elimination half-life
- › Efficacious, cost-effective & has applications for acute, chronic, neuropathic & cancer pain in adults & children
- › Low perioperative utilization despite decades of clinical use



Perioperative Methadone

Methadone achieves rapid [CNS effect site] : [plasma] equilibrium

- › Comparable to pharmacokinetics of sufentanil & fentanyl
- › By contrast, morphine can take up to 4 hrs

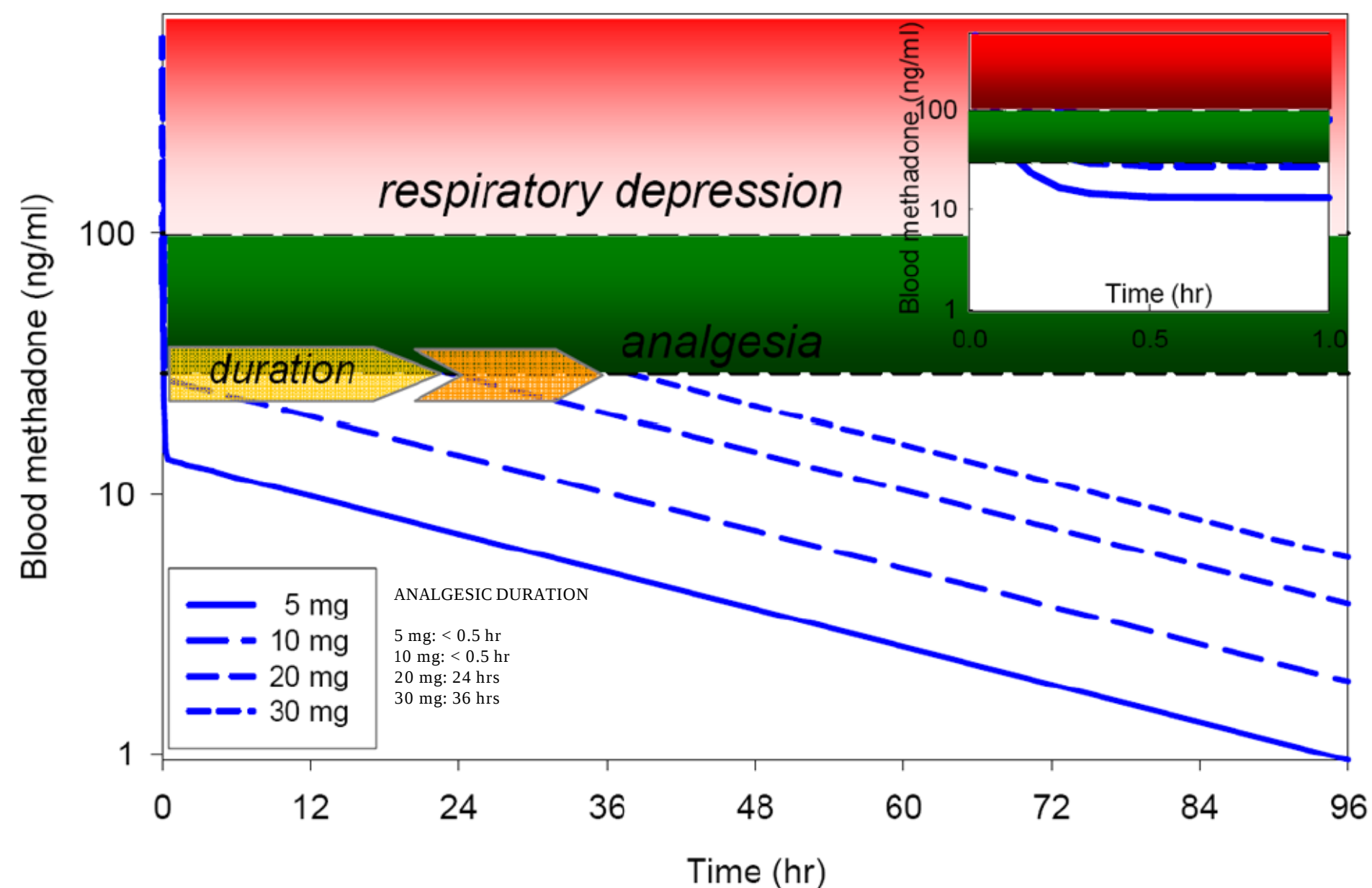
Opioid	Onset ($t_{1/2K_{e0}}$)	Elimination $t_{1/2}$
Remifentanyl	1 min	0.5 hr
Alfentanil	1 min	1 hr
Sufentanil	6 min	8 hr
Fentanyl	5 min	8-10 hr
Morphine	2-4 hr	2-3 hr
Methadone	8 min	24-36 hr



Perioperative Methadone

- Duration of analgesia depends on dose administered
 - › **Small dose** (<20 mg IV) duration determined by redistribution (half-life 5 min)
 - › **Larger dose** (20 mg or more IV) duration determined by systemic elimination (half-life 30 hrs); *expected duration of resp depression period less than 30-45 min (6 redistribution half-lives)
 - › **Goal of therapy**: target doses as high as possible above minimal analgesic concentration, but below respiratory depression threshold → longest analgesic duration
- Metabolism of methadone is controversial & likely less susceptible to inhibitory drug interactions (on CYP450s) than previously thought
 - › Recent studies suggest it is not a clinical substrate of CYP3A4, rather CYP2B6
- Methadone recommended regimen:
 1. **Methadone 20 mg IV bolus before induction (15 mg in older/high risk patients)**
 - › High risk = 'physiologically' older than 60 yo d/t DEC elimination & INC resp depression risk w/ age
 2. **Methadone 2-3 mg IV q >10 min prn postop pain**





Relationship between methadone dose & duration of effect. Minimal analgesic [plasma] = 30 ng/ml. Minimal respiratory depressant [plasma] = 100 ng/ml.

Perioperative Methadone

Gourlay et al. (Anesthesiology 1982, 1984, 1986) seminal work on perioperative use

- › Studies performed in orthopedic (anterior spinal fusion) and general surgery (open cholecystectomies)
- › Study designs included single dose methadone 20 mg IV w/ induction, methadone 20 mg IV w/ induction & methadone 5 mg IV in PACU/surgical ward prn postoperatively, & double-blind morphine vs methadone both intra- and post-operatively
- › **All studies demonstrated excellent & prolonged analgesia** (significant reductions in pain scores, increased time until requiring initial dose of postop opioid & reduced postop opioid consumption)
- › **No significant adverse events** (e.g. respiratory depression, dysrhythmias)
- › N/V incidence similar to comparator opioid agonists



Intraoperative Methadone Improves Postoperative Pain Control in Patients Undergoing Complex Spine Surgery

Antje Gottschalk, MD,*† Marcel E. Durieux, MD, PhD,* and Edward C. Nemergut, MD*

BACKGROUND: Patients undergoing complex spine surgery frequently experience severe pain in the postoperative period. The combined opiate receptor agonist/*N*-methyl-*D*-aspartate receptor antagonist methadone may be an optimal drug for these patients given the probable involvement of *N*-methyl-*D*-aspartate systems in the mechanism of opioid tolerance and hyperalgesia.

METHODS: Twenty-nine patients undergoing multilevel thoracolumbar spine surgery with instrumentation and fusion were enrolled in this prospective study and randomized to receive either methadone (0.2 mg/kg) before surgical incision or a continuous sufentanil infusion of 0.25 μ g/kg/h after a load of 0.75 μ g/kg. Postoperative analgesia was provided using IV opioids by patient-controlled analgesia. Patients were assessed with respect to pain scores (visual analog scale from 0 to 10), cumulative opioid requirement, and side effects at 24, 48, and 72 hours after surgery.

RESULTS: Demographic data, duration, and type of surgery were comparable between the groups. Methadone reduced postoperative opioid requirement by approximately 50% at 48 hours (sufentanil versus methadone group, median [25%/75% interquartile range]: 63 mg [27.3/86.1] vs 25 mg [16.5/31.5] morphine equivalents, $P = 0.023$; and 72 hours: 34 mg [19.9/91.5] vs 15 mg [8.8/27.8] morphine equivalents, $P = 0.024$) after surgery. In addition, pain scores were lower by approximately 50% in the methadone group at 48 hours after surgery (sufentanil versus methadone group [mean $\pm$ SD] 4.8 ± 2.4 vs 2.8 ± 2.0 , $P = 0.026$). The incidence of side effects was comparable in both groups.

CONCLUSION: Perioperative treatment with a single bolus of methadone improves postoperative pain control for patients undergoing complex spine surgery. (Anesth Analg 2011;112:218–23)

Ketamine is King!

- Rapid distribution into CNS
- Variable bioavailability: IM – 93%, IN 20-50%, PO 16-20%
- Elimination half-life of 10-15 min via CYP3A4
- Active metabolite, norketamine, 20-30% activity w/ *markedly prolonged* elimination half-life of 6 hr
 - › Undergoes glucuronidation & then excreted in urine
- MOA: NMDA receptor antagonist & KappaOR agonist
 - › NMDA receptor activation contributes to dorsal horn “wind-up” and central sensitization states (e.g., opioid tolerance & hyperalgesia) → ketamine antagonizes the NMDA receptor yielding improved analgesia



Perioperative Ketamine & Dexmedetomidine

- Perioperative dosing recommendations:

- › Ketamine 0.5 mg/kg IV bolus w/ induction (prior to incision)
- › Continuous infusion of 0.25 mg/kg/hr or intermittent boluses of 0.125 mg/kg q 30 min
- › Discontinue about 30 min before emergence to prevent clouding of extubation criteria
- › Discuss postop management of continuous infusion w/ surgeons

- Consider addition of **dexmedetomidine**:

- › Continuous infusion of 0.2-0.7 mcg/kg/hr
- › Discontinue about 30 min prior to emergence
 - › Context sensitive half-time 4 min after 10 min infusion increasing to 250 min after 8 hour infusion
- › Provides additional opioid sparing & attenuates sympathomimetic effects of ketamine



Evidence-Based Perioperative Pain Management

PROSPECT: PROcedure SPECific postoperative pain management (www.postoppain.org)

- › Evidence-based, procedure-specific guideline for perioperative pain management
- › Managed & developed by BOTH anesthesiologists & surgeons



- › Surgeries reviewed to date:
 - › TAH, lap cholecystectomy, TKA, THA, thoracotomy, radical prostatectomy, non-cosmetic breast surgery, herniorrhaphy, hemorrhoidectomy, colonic resection



Michigan OPEN Initiative

- **Acute pain** opioid prescriptions are high risk for misuse, diversion & adverse events because a lot go unused!
- Significant provider variation exists between what is prescribed (drug and amount) for the same acute pain condition
- Up to 10% of opioid naïve post-surgical patients become chronic opioid users!



Michigan OPEN Initiative

- Goals of program:
 - Reduce excess acute care opioid prescribing
 - Eliminate new persistent opioid use among postoperative and acute care patients
 - Reduce unintended opioid distribution into our local communities that leads to nonmedical use and abuse
 - Improve disposal practices to minimize the amount of unused opioids in our communities

Prescribing Recommendations

UPDATED 2019

Procedure	Oxycodone* 5mg tablets
Laparoscopic Cholecystectomy	10
Open Cholecystectomy	15
Appendectomy – Lap or Open	10
Hernia Repair – Major or Minor	10
Colectomy – Lap or Open	15
Ileostomy/Colostomy Creation, Re-siting, or Closure	15
Open Small Bowel Resection or Enterolysis	20
Thyroidectomy	5
Sleeve Gastrectomy	10
Prostatectomy	10
Laparoscopic Anti-reflux (Nissen)	10
Laparoscopic Donor Nephrectomy	10
Cardiac Surgery via Median Sternotomy	15

Procedure	Oxycodone* 5mg tablets
Hysterectomy – Vaginal, Lap/Robotic, or Abdominal	15
Cesarean Section	15
Breast Biopsy or Lumpectomy	5
Lumpectomy + Sentinel Lymph Node Biopsy	5
Sentinel Lymph Node Biopsy Only	5
Wide Local Excision ± Sentinel Lymph Node Biopsy	20
Simple Mastectomy ± Sentinel Lymph Node Biopsy	20
Modified Radical Mastectomy or Axillary Lymph Node Dissection	30
Carotid Endarterectomy	10
Total Hip Arthroplasty	30
Total Knee Arthroplasty	50
Dental	0

*The recommendations remain the same if prescribing hydrocodone 5mg

Postop Prescribing Recommendations

- Humana-sponsored
- JHU inter-professional working group
- Recs for opioid naïve patients

Surgical procedure	Open hysterectomy
Pre-operative	1 g PO acetaminophen/300 mg PO gabapentin
Intra-operative	IV ketorolac 15 – 30 mg one time (at conclusion of surgery)
Postoperative standing orders	1. Acetaminophen 1 g PO every 8 hours for first week - 1 g PO acetaminophen every 12 hours for second week - 1 g PO acetaminophen prn for pain after second week 2. Ibuprofen (NSAIDs) 400 mg every 8 hours for 3 days, followed by prn for pain 3. Gabapentin 100 mg PO twice a day for one week - Gabapentin 100 mg PO at bed time for 14 days
Postoperative narcotic PRN only: Prescribe one only	◇ Tramadol 50 mg every 6 hours prn for 7 days = 28 pills (MME = 20mg) ◇ Oxycodone 5 mg PO every 12 hours prn for 7 days = 14 pills (MME = 15mg) ◇ Dilaudid 4 mg PO every 12 hours prn for 7 days = 14 pills (MME = 32mg)
Surgical procedure	Robotic retro pubic prostatectomy
Pre-operative	1 g PO acetaminophen/300 mg PO gabapentin
Intra-operative	IV ketorolac 15 – 30 mg one time (at conclusion of surgery)
Postoperative standing orders	1. Acetaminophen 1 g PO every 8 hours for first week - 1 g PO acetaminophen every 12 hours for second week - 1 g PO acetaminophen prn for pain after second week 2. Ibuprofen (NSAIDs) 400 mg every 8 hours for 3 days, followed by prn for pain 3. Gabapentin 100 mg PO twice a day for one week - Gabapentin 100 mg PO at bed time for 14 days 4. Lidoderm patch every 12 hours at the site of laparoscopic incision
Postoperative narcotic PRN only: Prescribe one only	◇ Tramadol 50 mg every 6 hours prn for 5 days = 20 pills (MME = 20mg) ◇ Oxycodone 5 mg PO every 12 hours prn for 5 days = 10 pills (MME = 15mg) ◇ Dilaudid 4 mg PO every 12 hours prn for 5 days = 10 pills (MME = 32mg)

SET EXPECTATIONS: “Some pain is normal. You should be able to walk and do light activity, but may be sore for a few days. This will gradually get better.”

SET NORMS: “Half of patients who have this procedure take under 10-15 pills.”

NON-OPIOIDS: “Take acetaminophen and ibuprofen around the clock, and use the stronger pain pills only as needed for breakthrough pain.”

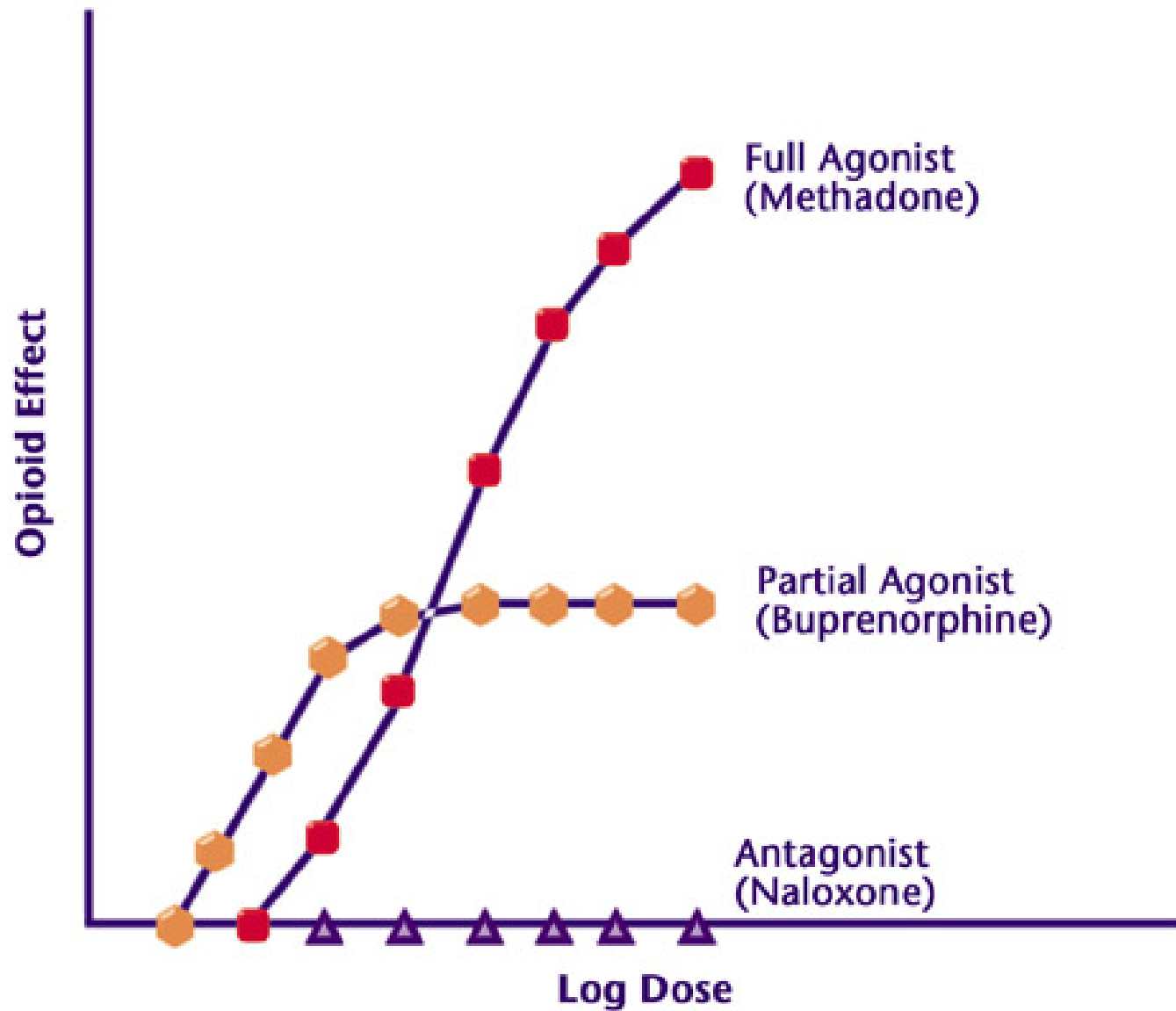
Avoid NSAIDs in patients with peptic ulcer disease and associated risk factors (smoking, drinking), bleeding disorders, renal disease, and specific operations at surgeon discretion.

APPROPRIATE USE: “These pills are for pain from your surgery, and should not be used to treat pain from other conditions.”

ADVERSE AFFECTS: “We are careful about opioids because they have been shown to be addictive, cause you harm, and even cause overdose if used incorrectly or abused.”

SAFE DISPOSAL “Disposing of these pills prevents others, including children, from accidentally overdosing. You can take pills to an approved collector (including police stations), or mix pills with kitty litter in a bag and throw them in the trash.”

Implications of Medication Assisted Treatment on Perioperative Analgesic Care



Patients on Methadone

- Continue baseline methadone dose if possible
 - › Usually dosed BID or TID for chronic pain
 - › Typically dosed once daily for opioid addiction
- Abrupt discontinuation can make providing adequate analgesia more difficult
- If patients are NPO, convert to IV methadone or seek expert opinion on converting to another opioid that is appropriate
- If *> 200 mg/day*, check ECG as *increased risk of QT prolongation*

Patients on Buprenorphine

- MuOR partial agonist, kappa- & deltaOR antagonist
 - › **High affinity for opioid receptors w/ slow dissociation**
 - › Occupies MuOR almost maximally leaving few available
 - › Lower intrinsic binding capacity compared to full agonists
 - › Rapid onset (highly lipophilic) – 5-15 min IV/IM, 15-45 min SL
 - › Long duration of effect of 6-8 hr
 - › Metabolism via CYP450
 - › Metabolite, norbuprenorphine, w/ 25% analgesic activity, but 10 times respiratory depression
 - › Terminal elimination in bile & urine after glucuronidation
- Potent analgesic w/ no analgesic ceiling effect
- Antihyperalgesic effects stronger than analgesic effects
- No respiratory depression up to 10 mg, ceiling effect w/ higher doses

Buprenorphine, continued

- Routes of administration

- › IV, SL, TD, IM, SC, epidural, intrathecal, intraarticular, perineural

- Dosing

- › IV 5-15 mcg/kg; onset 5-15 min; provides analgesia up to 13 hr
 - › 0.3 mg equianalgesic to 10 mg morphine in non-opioid dependent patients
- › SL 0.2-0.4 mg; onset 15-45 min
 - › Subutex (buprenorphine only), Suboxone (buprenorphine + naloxone)
- › TD (35, 52.5 & 70 mcg/hr) q 7 days; onset is 12-24 hr

- Perioperative management strategies:

- › Convert to full opioid agonist preoperatively (at least 72 hrs) & use full agonist perioperatively
 - › Use methadone or other long-acting opioid for baseline pain
- › Continue baseline buprenorphine & use full agonist periop
- › Continue baseline buprenorphine & use IV/SL buprenorphine periop

Questions?



