Acute Pain Management in Family Dental Medicine

Increasing the armamentarium of acute pain therapy

Colin Reeve, BSP, CTE,CDE

Disclosures

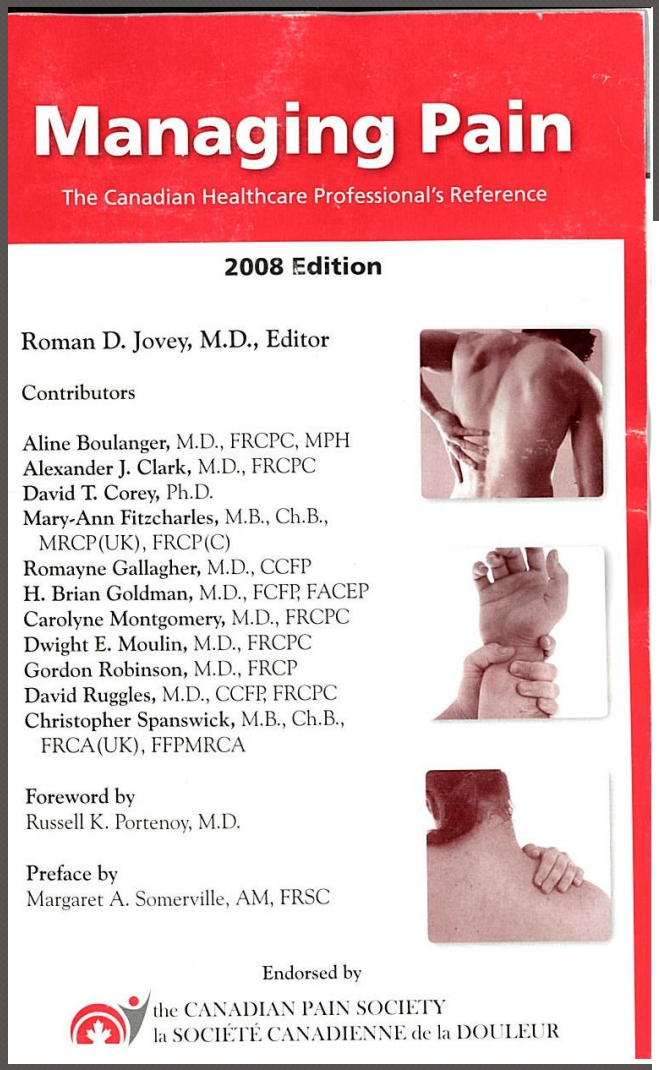
- None

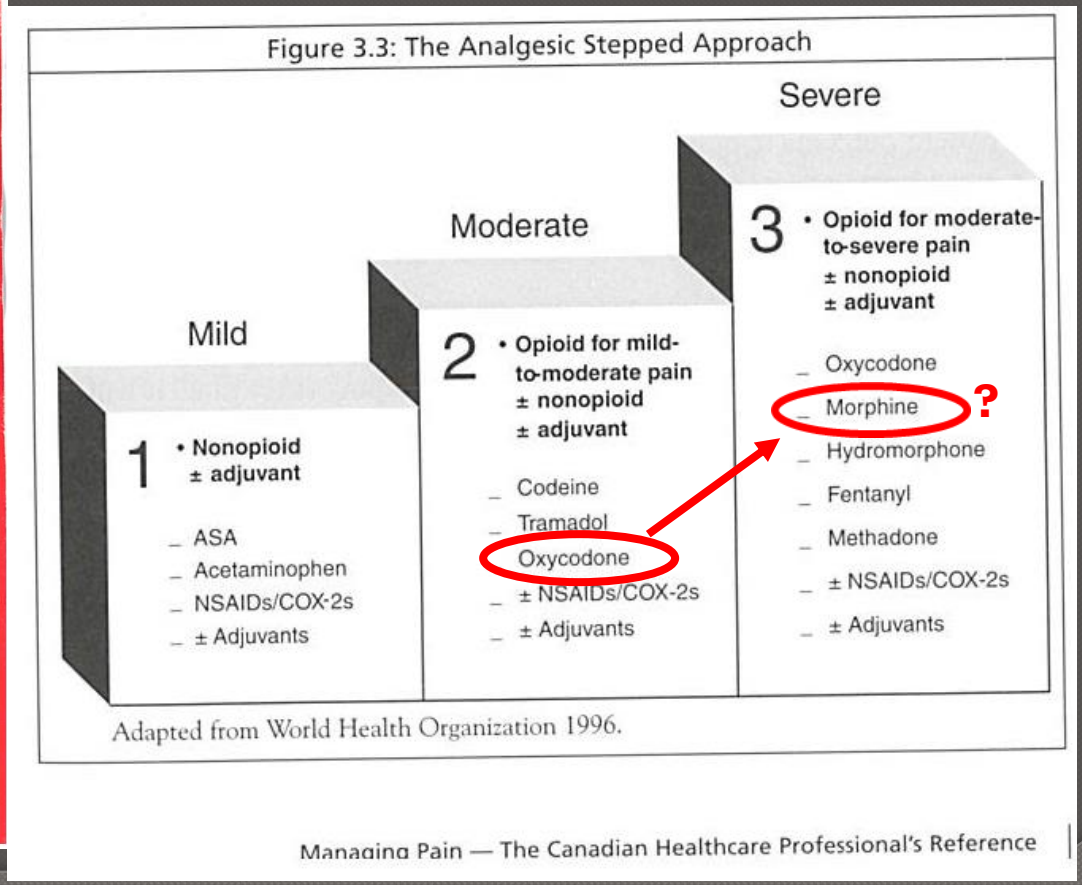
Learning Objectives

- By the end of this presentation, you will be able to:
  - Describe effective treatment options for acute pain secondary to oral operative procedures
  - List contraindications to commonly prescribed acute pain therapies
  - Compare and contrast appropriate analgesic options for a specific patient case
  - Identify potential aberrant (drug seeking) behavior in a patient requesting opioid therapy

The changing landscape of analgesic therapy

Where do you go for accurate, unbiased information?





Recent/future advancements in analgesic therapies

Figure 1 Distribution by Indication

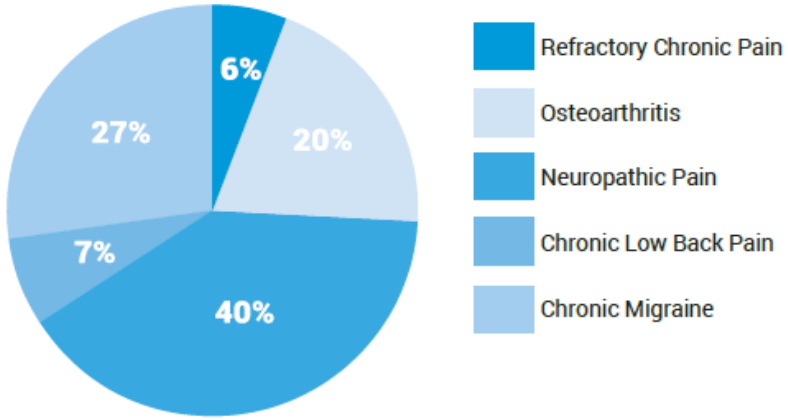
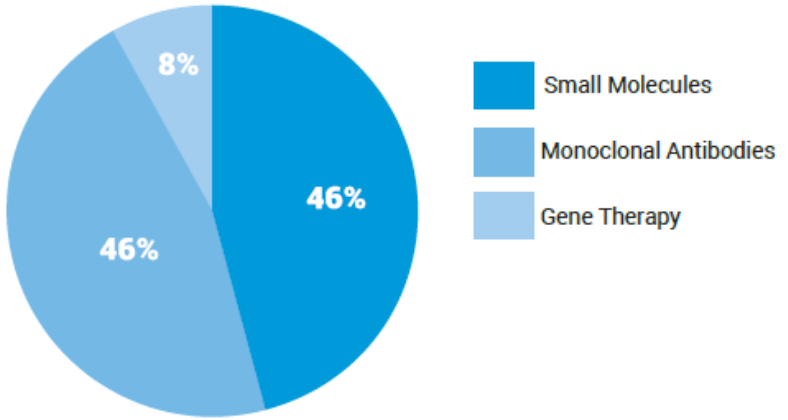


Figure 2 Distribution by Molecule Type

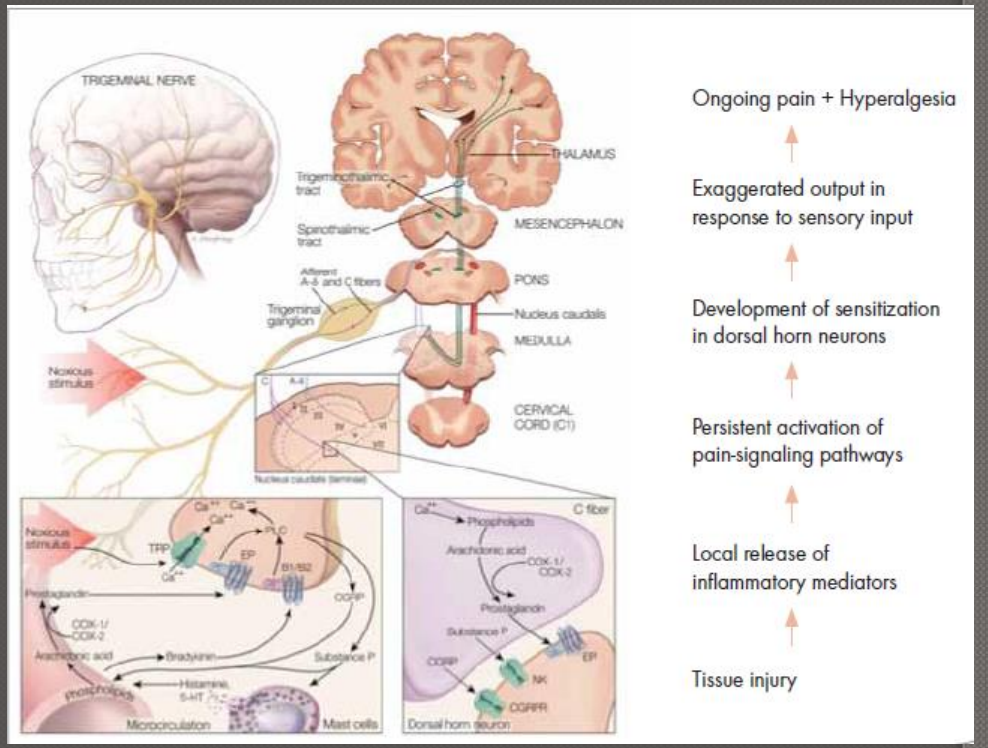


- Recent additions to the Canadian market include:
  - Partial Mu agonist antagonists
    - Buprenorphine
  - Tamper/abuse resistant formulations:
    - Oxyneo®
    - Addition of Naloxone to tablet formulation
  - Synthetic Opioids:
    - Tapentadol
    - Tramadol

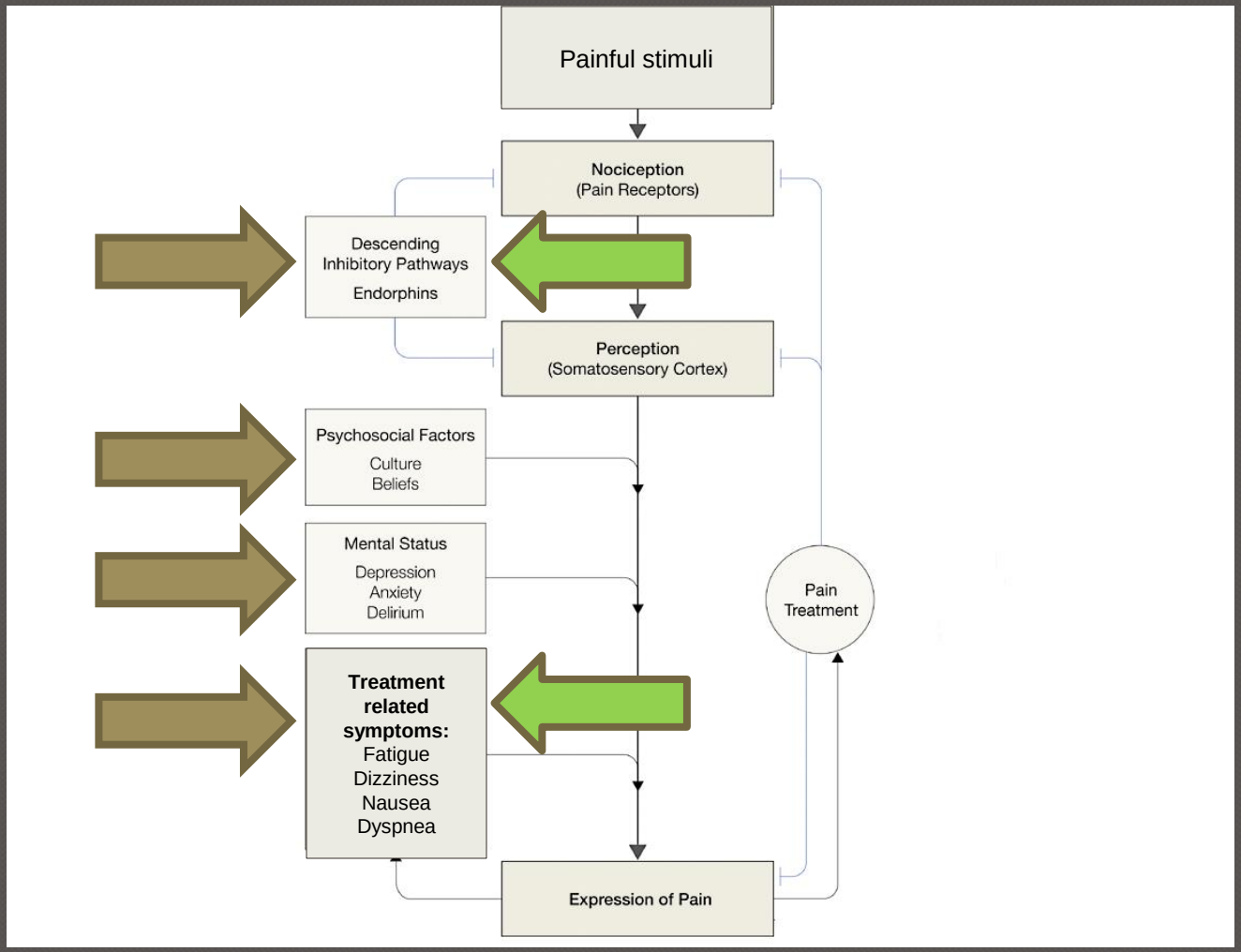
https://www.cadth.ca/emerging-non-opioid-drugs-treatment-pain

(Acute) Dental Pain

- Classified as Musculoskeletal Pain
- Postsurgical dental pain is at its peak within 6–8 hours following a procedure
- Postoperative dental pain and other functional sequelae, (reduced mouth opening and facial swelling) will be most significant for approximately two to three days, after which it is expected to diminish
- Most operative procedures will result in mild-moderate to moderate-severe pain with some level of inflammation

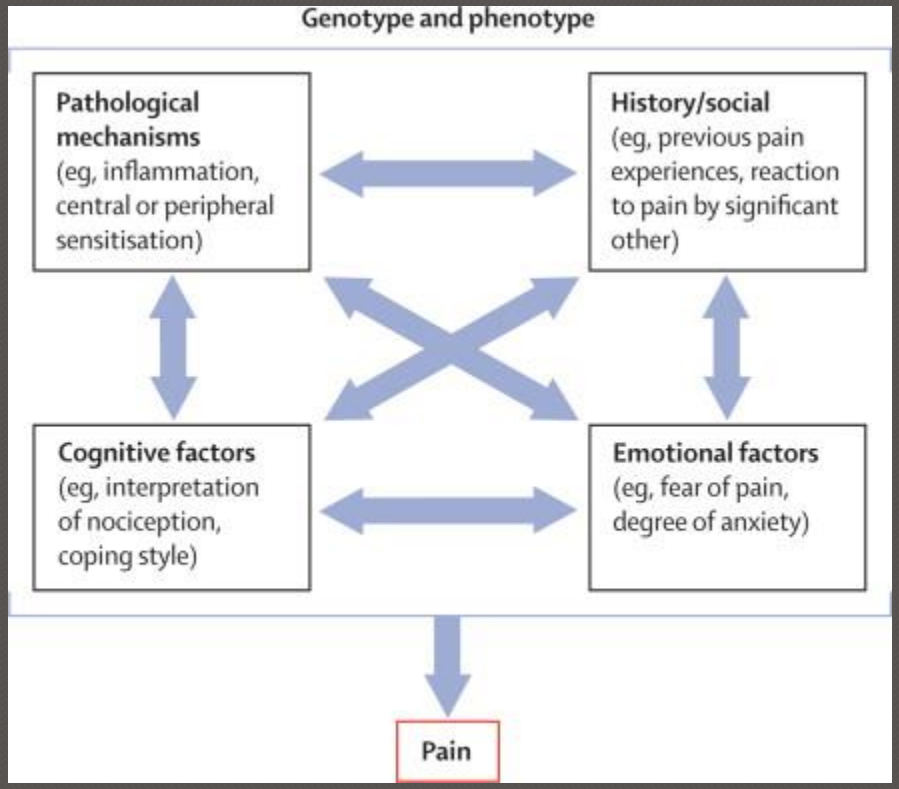


Considerations in Acute Pain Management



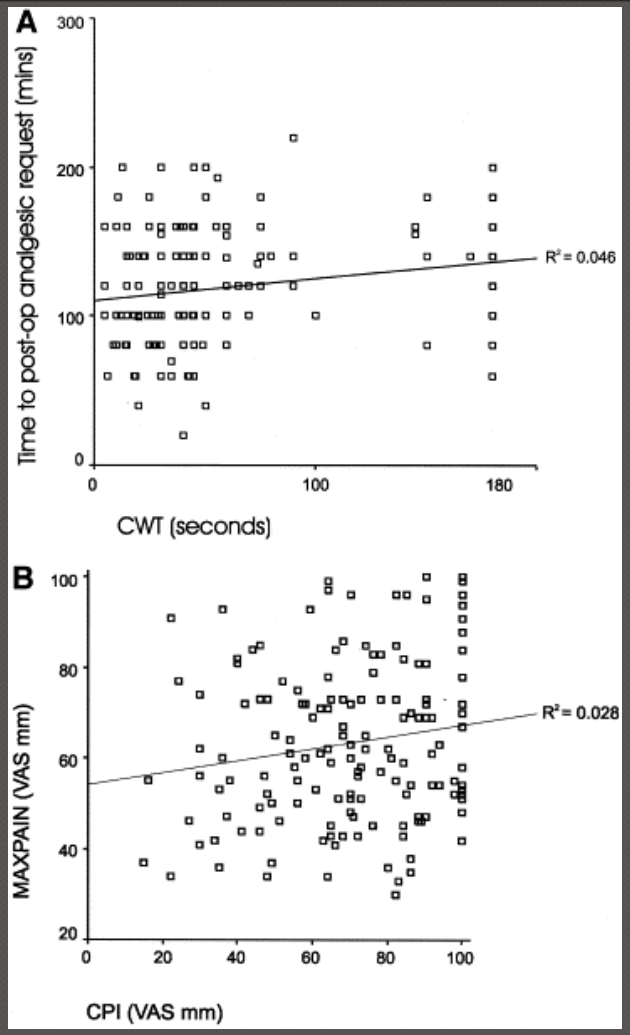
Adapted from: Bruera, E. et al. JAMA 2003;290:2476-2479

Genotype vs Phenotype



Dennis C Turk, Hilary D Wilson, Alex Cahana, Treatment of chronic non-cancer pain, The Lancet, Volume 377, Issue 9784, 2011,Pages 2226-2235,

Heterogeneity of pain phenotypes



- N = 617; 369 women, 248 men exposed to experimentally induced pain including thermal stimuli and the cold pressor test to delineate individual response patterns and pain phenotypes.
- A subset of subjects (n = 157; 99 women and 58 men) also underwent standardized oral surgery, and the responses to clinically induced acute inflammatory pain were evaluated
- Pain reported following the removal of two partially impacted third molars by the same oral surgeon under carefully controlled conditions ranged from slight to severe pain.

Kim H, Neubert JK, Rowan J, Brahim J, Iadarola MJ,Dionne RA. Comparison of experimental and acute clinical pain responses in humans as pain phenotypes. J Pain 2004;5:377-384.

How do we choose the most effective (and safe) acute pain therapy?

- The PAIN Prevention Paradigm:

P Prevent: attenuating the development of hyperalgesia due to the development of sensitization in pain-sensing neurons

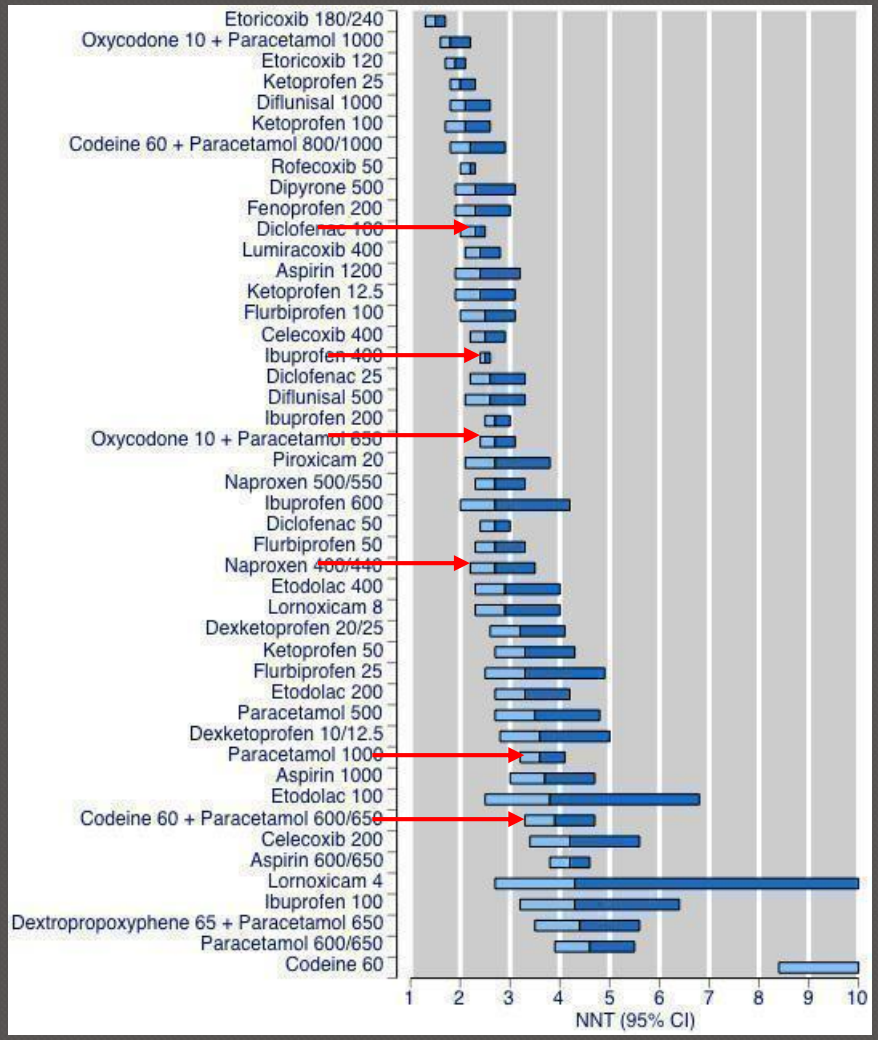
A Anti-inflammatory: Administration of an NSAID in the preoperative period allows sufficient time for drug absorption during the procedure and the one to two hours of local anesthetic duration postoperatively.

I Individualize: Abandon the “one-size fits-all” paradigm for pain management.

N Narcotic: Consider the addition of an opioid with NSAID therapy if insufficient pain management or as monotherapy in the event of a CI to NSAID therapy

Adapted from:R. A. Dionne, S.M. Gordon, Changing Paradigms for Acute Dental Pain: Prevention Is Better Than PRN, CDA JOURNAL, VOL 43, N°11

Single dose oral analgesics for acute postoperative pain in adults



Dental pain: NNT for at least 50% maximum pain relief over four to six hours compared with placebo, by rank order.

Cochrane Database of Systematic Reviews 7 SEP 2011 DOI: 10.1002/14651858.CD008659.pub2

Pre-operative NSAID

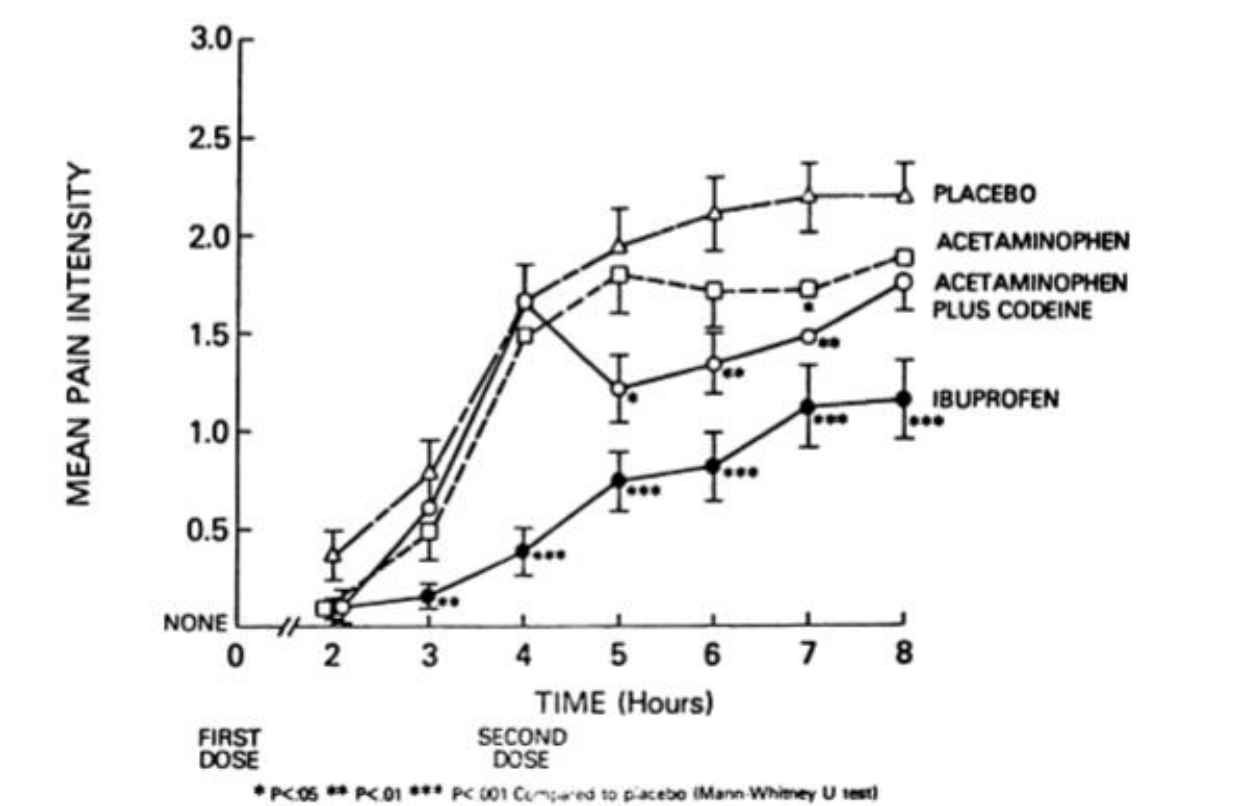


Fig. 1. Time–effect curves for placebo, 400–800 mg ibuprofen, 600 mg acetaminophen, and 600 mg acetaminophen plus 60 mg codeine. Mean pain intensity scores are plotted v. time in hours from first dose.

DIONNE RA, CAMPBELL RA, COOPER SA, HALL DL, BUCKINGHAM B. Suppression of Postoperative Pain by Preoperative Administration of Ibuprofen in Comparison to Placebo, Acetaminophen, and Acetaminophen Plus Codeine. The Journal of Clinical Pharmacology 1983;23(1):37-43

Case: KD

- KD, a 28 Yo Caucasian male
- Bone graft and implant with out complications; local anesthesia
- PMHx:
  - Asthma

You provide him with a prescription for: Tylenol#3: 1-2 tabs q 4-6 h prn pain

KD states: "Nothing works for my pain, I need something stronger, what else can you give me for my pain?"

Case: KD

- What are our options for oral analgesia in acute dental pain?

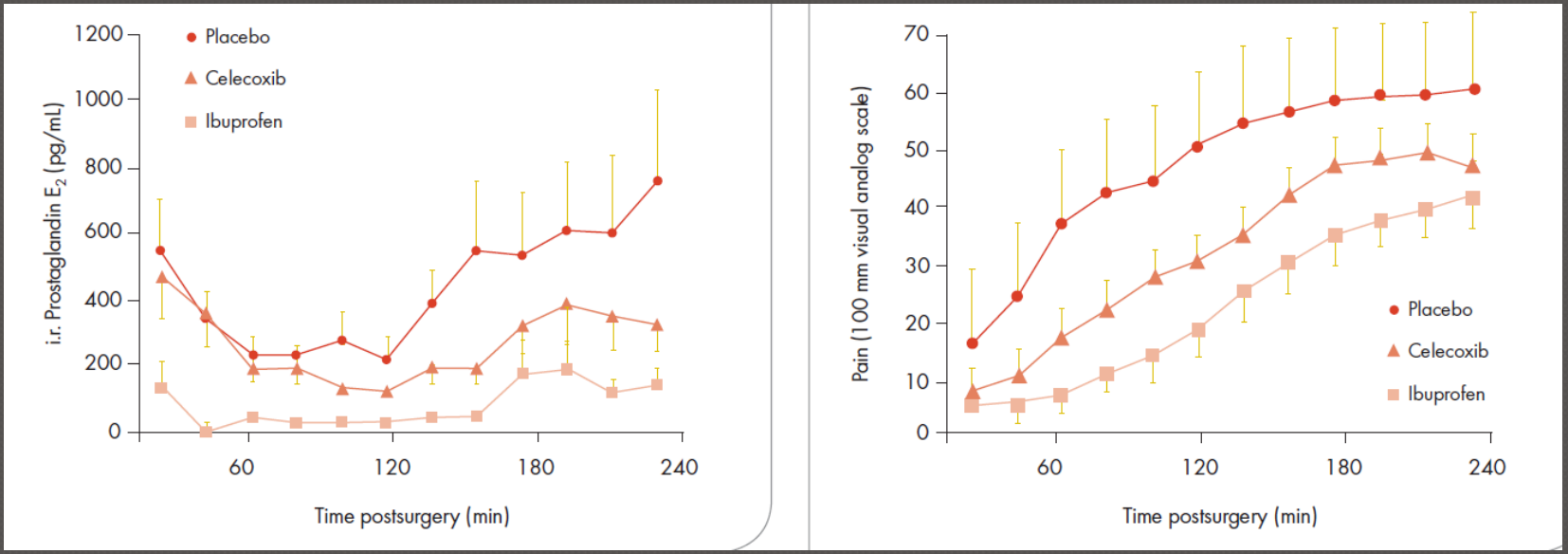
Medication Class	Relative Effectiveness in Pain States
Nonsteroidal antiinflammatory drugs	Tissue injury >> acute stimuli = nerve injury = 0
Opioids (μ agonists)	Tissue injury = acute stimuli > nerve injury > 0
~~Anticonvulsants~~	~~Nerve injury > tissue injury = acute stimuli = 0~~

Constantinos Laskarides, Update on Analgesic Medication for Adult and Pediatric Dental Patients, Dental Clinics of North America, Volume 60, Issue 2,2016,Pages 347-366

NSAIDS

- NSAIDs work by inhibiting cyclooxygenase (COX 1&2) and subsequent prostaglandin synthesis as well as by other less understood mechanisms (possibly via the endogenous opioid system)
- Possess analgesic, anti-inflammatory, antipyretic and antithrombotic properties
- **About 60% of patients** will respond to a specific NSAID; non-responders are just as likely to respond to an alternate agent particularly if it is from a different chemical class
- **Wide variability in patients' response** may be due to differences in pain threshold, disease severity, cyclooxygenase configuration, and other factors

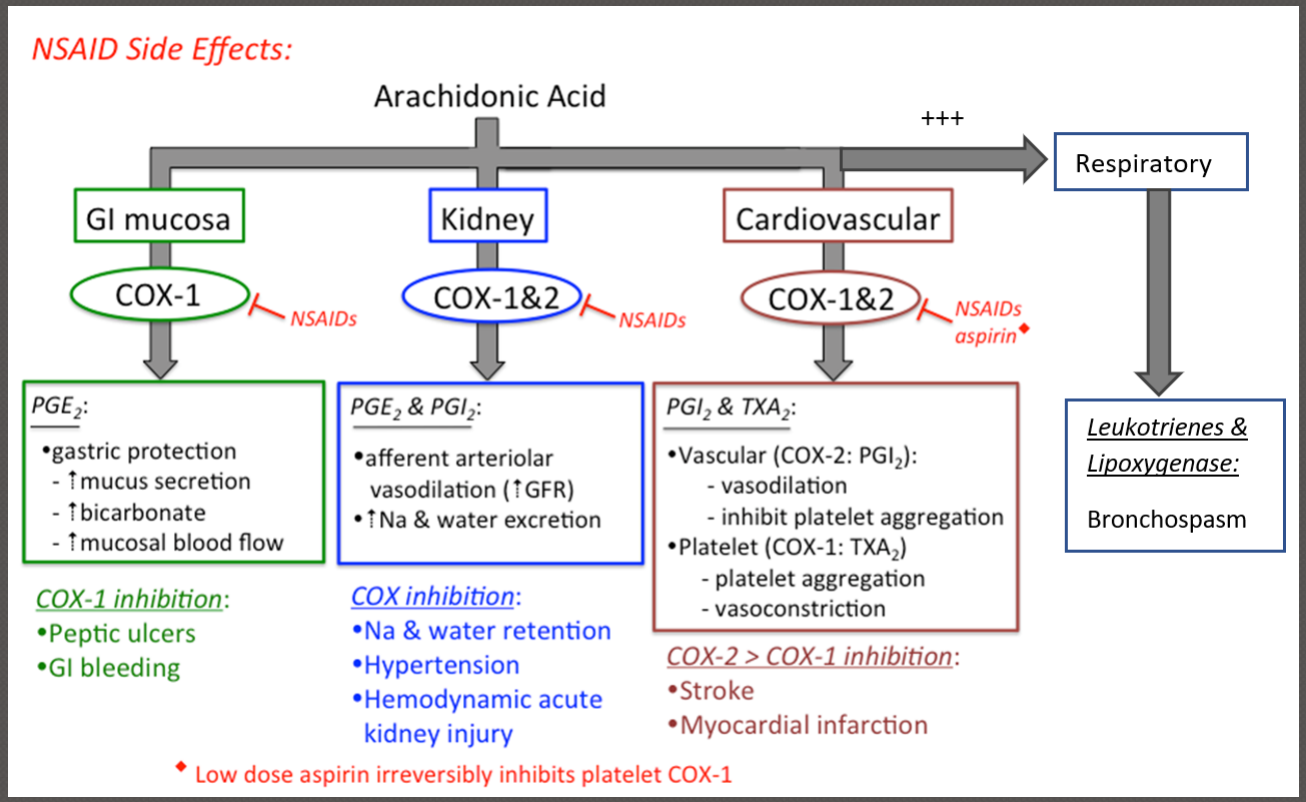
NSAID



The relationship between peripheral levels of prostaglandin E2 (PGE2) and the onset of pain following tissue injury (the removal of impacted third molars).

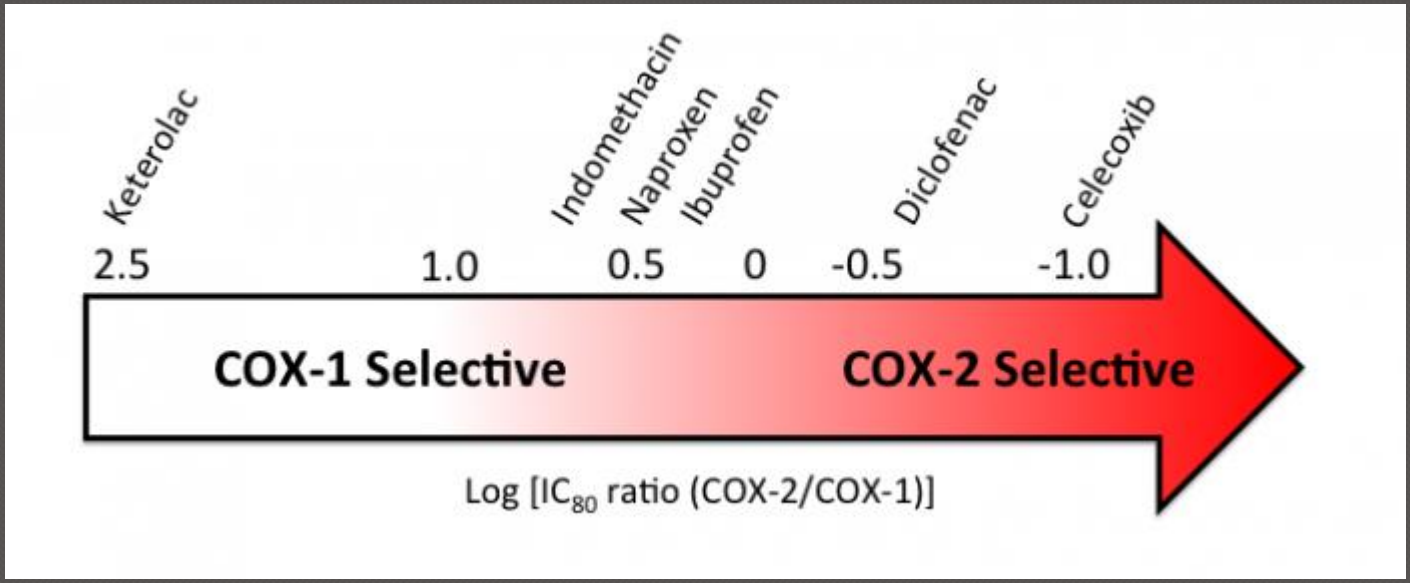
Khan AA et al. Clin Pharmacol Therap 2002; 72:44-49).

Contraindications to NSAID use



Adapted from: http://tmedweb.tulane.edu/pharmwiki/lib/exe/fetch.php/nsaid_harm.png?w=700&tok=b8e648

NSAID


Keterolac
Indomethacin
Naproxen
Ibuprofen
Diclofenac
Celecoxib
2.5
1.0
0.5
0
-0.5
-1.0
COX-1 Selective
COX-2 Selective
Log [IC80 ratio (COX-2/COX-1)]

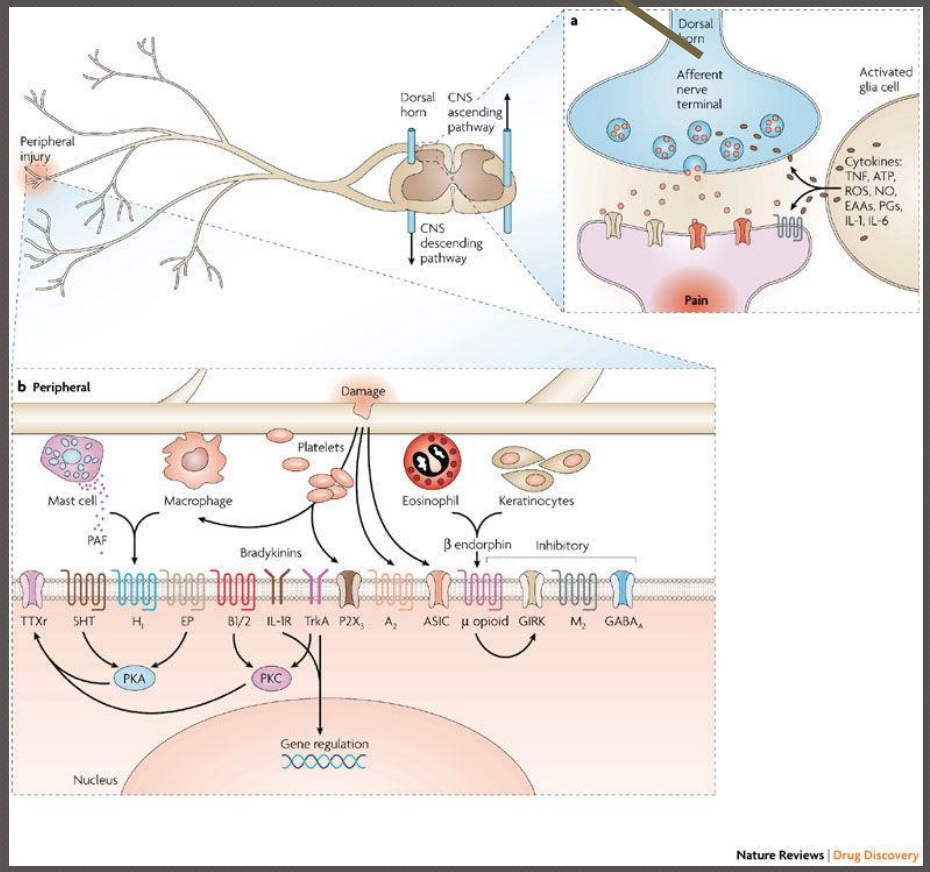
Case: KD

- KD reveals that he previously took Tylenol#3's for a back injury with no pain relief (he experienced +++constipation); the pain was subsequently responsive to physical rehab and acetaminophen therapy
- KD suffers from seasonally exacerbations of asthma. He is currently using his "blue puffer" two puffs 5-6 times daily

Opioids

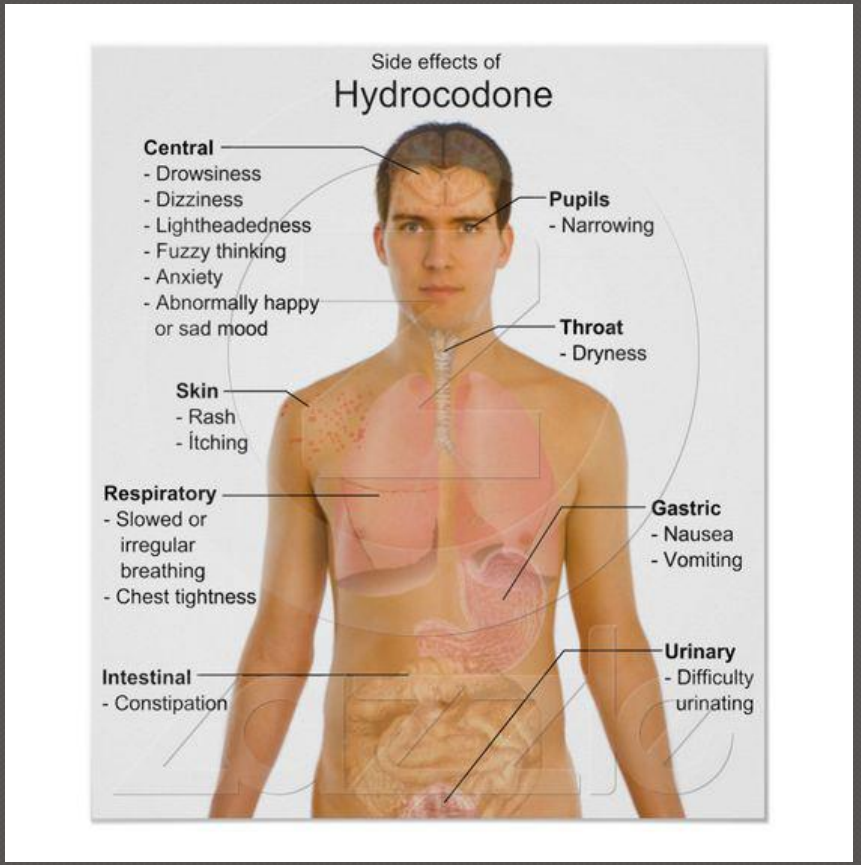
Opioid receptors are densely found in the dorsal horn of the spinal cord
Act by causing hyperpolarization of neurons reducing excitability and modulating pain transfer

- Opioid analgesics act primarily on the CNS and the intestines
- The perception of and emotional response to pain are modified when opioid analgesics bind with stereospecific receptors in the CNS

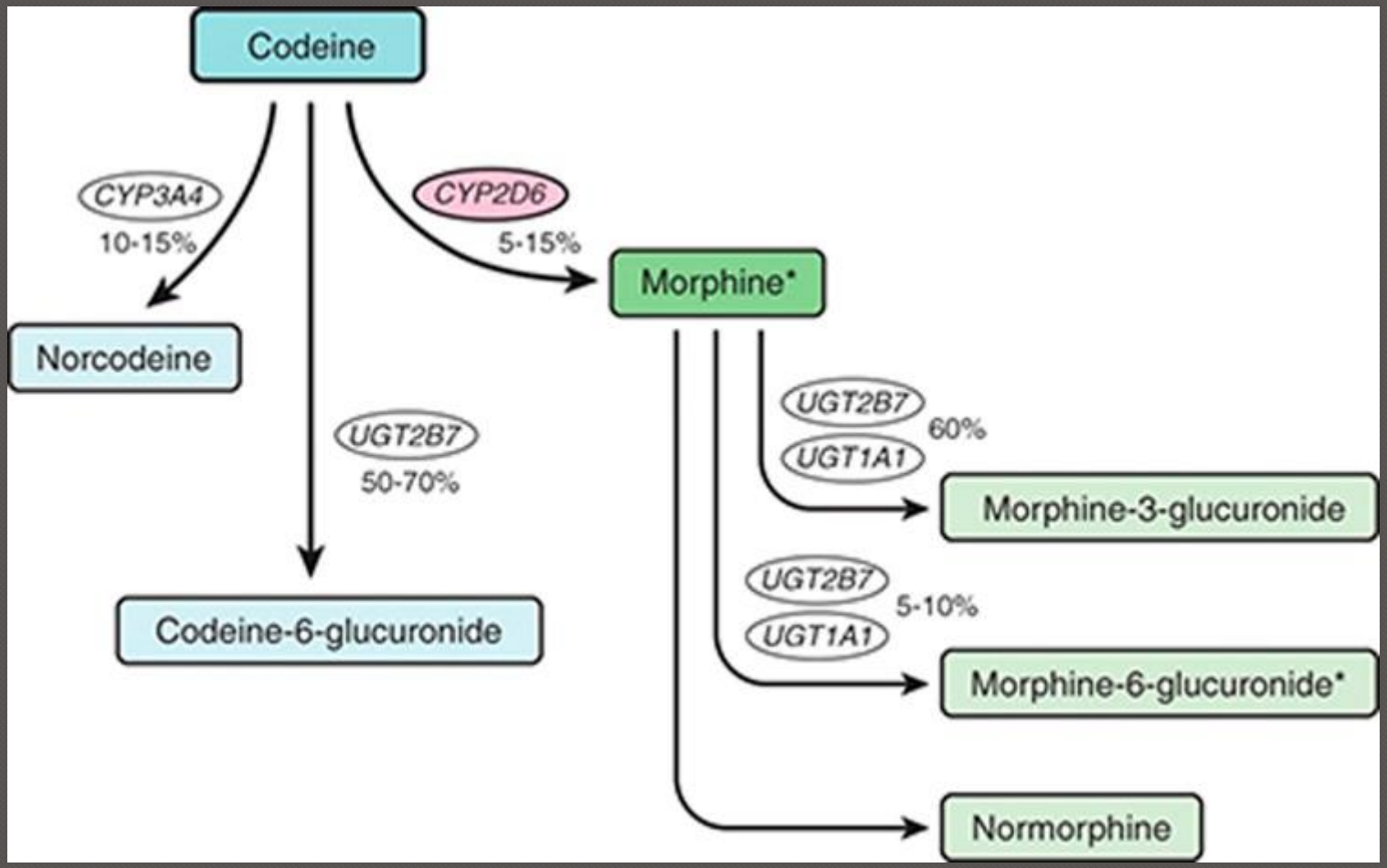


Opioid Side Effects

- Common (>15%):
  - CNS: drowsiness, dizziness, vertigo
  - Derm: dry-skin, itching, pruritus
  - GI: nausea, constipation, and vomiting
- ~80% of patient's receiving opioid therapy will experience at least 1 side effect!



Codeine Metabolism



Codeine Metabolism

Likely phenotype[a]	Activity score	Genotypes	Examples of diplotypes
Ultrarapid metabolizer (~1–2% of patients)	>2.0	An individual carrying more than two copies of functional alleles	*1/*1xN, *1/*2xN
Extensive metabolizer (~77–92% of patients)	1.0–2.0[b]	An individual carrying two alleles encoding full or reduced function; or one full-function allele together with either one nonfunctional or one reduced-function allele	*1/*1, *1/*2, *2/*2, *1/*41, *1/*4, *2/*5, *1/*10
Intermediate metabolizer (~2–11% of patients)	0.5[b]	An individual carrying one reduced-function and one nonfunctional allele	*4/*10, *5/*41
Poor metabolizer (~5–10% of patients)	0	An individual carrying no functional alleles	*4/*4, *4/*5, *5/*5, *4/*6

[a]The frequency estimates are based on data from Caucasians and may differ substantially for other ethnicities. See **Supplementary Data** online for estimates of phenotype frequencies among different ethnic/geographic groups. [b]Note that some investigators define patients with an activity score of 0.5 and 1.0 as intermediate metabolizers and those with an activity score of 1.5 and 2.0 as extensive metabolizers. Classifying patients with an activity score of 1.0 as extensive metabolizers in this guideline is based on data specific for formation of morphine from codeine in these patients.[12]

ClinPharmacolTher2014; 95(4):376

Ultrametabolism of Codeine

- "A newborn male infant, born after an unremarkable pregnancy and delivery (birth weight 3.88 kg, 90th percentile), developed difficulty breastfeeding and increasing lethargy at 7 days of age. At 11 days of age, he was taken to a pediatrician owing to concerns about his skin colour and decreased milk intake. The pediatrician noted that the infant had gained his birth weight. Subsequently, on day 13, an ambulance team found the baby cyanotic and without vital signs. Resuscitation, which was initiated at home and continued in the hospital's emergency department, was unsuccessful"

Ultrametabolism of Codeine

- "Review of the medical records revealed that in the immediate postpartum period the mother was prescribed Tylenol® 3 (codeine 30 mg and acetaminophen 500 mg). Initially she took 2 tablets twice daily, but she halved the dose on postpartum day 2 owing to somnolence and constipation. Following the development of poor neonatal feeding, the mother expressed milk and stored it in a freezer. Analysis of the milk for morphine using a specific enzyme-linked immunosorbent assay method for morphine revealed a concentration of 87 ng/mL."

Opioid Screen

McMaster University
Inspiring Innovation and Discovery

Opioid Risk Tool

Item	Mark each box that applies	Item score if female	Item score if male
1. Family History of Substance Abuse:			
Alcohol	[ ]	1	3
Illegal Drugs	[ ]	2	3
Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse:			
Alcohol	[ ]	3	3
Illegal Drugs	[ ]	4	4
Prescription Drugs	[ ]	5	5
3. Age (mark box if 16-45)	[ ]	1	1
4. History of Preadolescent Sexual Abuse	[ ]	3	0
5. Psychological Disease			
Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar, Schizophrenia	[ ]	2	2
Depression	[ ]	1	1
Total		____	____
Total Score Risk Category: Low Risk: 0 to 3 Moderate Risk: 4 to 7 High Risk: 8 and above			

Opioid Screen

- Recognize drug seeking signs
  - Allergic to weak opioids or NSAIDs
  - Knows clinical terms and street names for prescription drugs
- Request specific drugs& have perfect story - It's OK to say "No"
- Signs of intoxication or abuse
- Check electronic prescription drug profile &/or contact previous or current regular practitioner
- Ask if patient has an opioid contract with a provider

Case: KD

- You perform an opioid risk assessment which is unremarkable
- You empirically assess KD as a possible non-metabolizer of codeine based on his ethnicity and past history of nil response to codeine therapy
- You decide to start KD on:
  - Morphine 5mg IR q 4-6h prn (max 8 tablets per day) X 5days co-administered with acetaminophen 500mg 1-2 tablets q 4-6 hours

Case: JS

- JS is a 68 Yo overweight Caribbean female requiring root canal
- PMHx
  - LBP (NYD)
  - HTN (BP 115/72)
  - DM2
  - OSA (CPAP therapy "most" nights)
- Current Medications:
  - Amlodipine 10mg once daily
  - ASA EC 81mg once daily
  - Gliclazide MR 60mg once daily
  - Metformin 1000mg twice daily
  - Hydromorphone CR 9mg twice daily (increased from 6mg twice daily one week prior due to uncontrolled pain)
  - Hydromorphone IR 1mg 1-2 tablets once to twice daily prn b/t pain (typically 4 tablets per day)

Case JS

- While performing a dental examination, JS reports +++pain (jaw, back, feet); manipulation of the oral cavity with dental instrumentation causes +++pain (a 10/10); JS wants to be "put under" for the procedure repeatedly stating fears of increasing her pain status further with the root canal procedure

Case: JS

What can you do to help minimize JS' post-procedure pain?

From: **Opioid Dose and Drug-Related Mortality in Patients With Nonmalignant Pain**

Arch Intern Med. 2011;171(7):686-691. doi:10.1001/archinternmed.2011.117

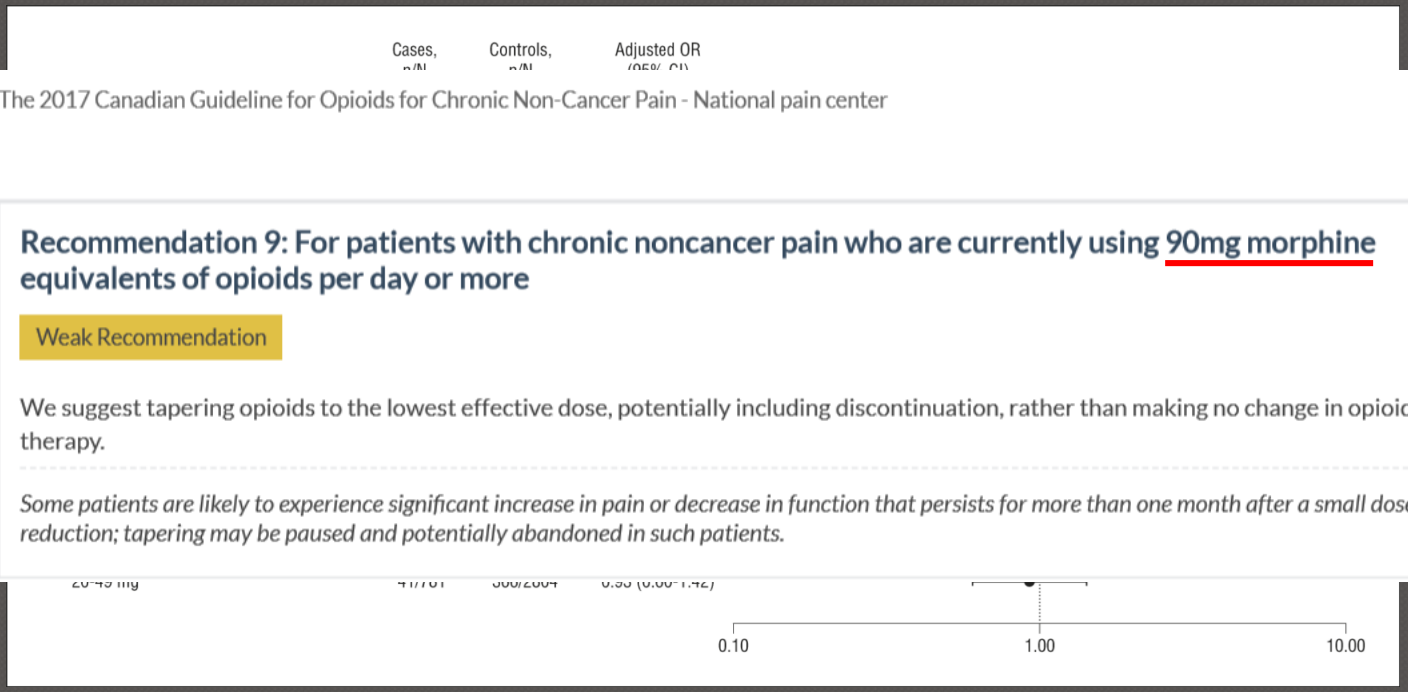


Figure Legend:

Association between opioid-related death and opioid dose. Adjusted for previous drug use (selective serotonin reuptake inhibitors, other antidepressants, benzodiazepine, other psychotropic drugs and central nervous system depressants, and methadone), the number of drugs used in past 6 months, duration of opioid treatment, the number of physicians prescribing opioids, the number of pharmacies dispensing opioids, and the presence of any long-acting opioid dispensed in exposure window. CI indicates confidence interval; OR, odds ratio.

Opioid Conversion Table

	To convert to oral morphine Multiple by:	To convert from oral morphine Multiple by:	Equivalent to 30mg morphine (mg)
Morphine	1	1	30
Codeine	0.15	6.67	200
Oxycodone	1.5	0.667	20
Hydromorphone	5	0.2	6

Opioid Related Respiratory Effects

- Tolerance to the respiratory depressant effects of opioids develops slowly and incompletely
- OSA:
  - • Prevalence ~ 24%
  - • Risk is linearly related to escalating morphine equivalent daily dose
  - • Risk factors: dose, normal body weight, benzodiazepine
  - • Benzodiazepine/hypnotics depress central nervous system activity and blunt the arousal or ventilatory response to hypoxia and hypercapnia

Anesth Analg. 2015 Jun;120(6):1273-85

Hyperalgesia

- State of nociceptive sensitization caused by exposure to opioids characterized by a paradoxical response
- Mechanism not yet understood,
- More common for high opioid doses
- Clinical features: increasing pain despite increasing doses; pain
- more diffuse; pain extending beyond distribution of pre-existing pain

Case: JS

- You decide to start JS on a pre-operative dose of Ibuprofen 400mg (2 hours before procedure) continuing q 4-6h regular dosing with acetaminophen 500-1000mg q4-6hr prn for b/t pain
- You instruct JS to take the first dose of the day 1 hour prior to her daily ASA

Tips and pearls

- Temper patient's expectation of "pain relief" to "pain reduction" therapy
- NSAIDs such as Ibuprofen 400-600mg QID or naproxen 375-500mg BID are often as/more effective than alternative weak/combination opioids such as Tylenol #3, Percocet, and even low doses of potent opioids
- Role for short-term regular dosing of NSAIDs or acetaminophen when pain expected to be constant over a few days (e.g. take regular for 5 days, then prn)
- Consider pre-op dosing of NSAIDs to pre-emptively inhibit COX-2 production perioperatively/post-op

Questions?

For Reference

	Generic Name (Brand Name)	Relative Histamine Release	Equianalgesic Dose in Adults (oral)	MEQ (Oral Morphine equivalent)	Comments
Strong Opioids	**Phenanthrenes (morphine-like agonists)**				
	Morphine M.O.S; MS-IR; Statex, MS Contin	+++	20-30mg	1	-Gold standard -Avoid if CrCl <20-30ml/min
	Hydromorphone (Dilaudid, Hydromorph Contin)	+	4-6mg (as high as 7.5mg; bioavailability varies	5	-May have ↓ AEs than morphine
	Oxycodone (Oxyneo, Oxy-IR)	+	10-20mg; up to 30mg	1.5	Percocet=oxycodone 5mg + acet.325mg].
	Phenylpiperidines				
	Fentanyl (Duragesic, various)	+	0.1 25mg (Variable)	N/A	Do not use in opiate naive or acute pain
Weak Opioids	**Phenanthrenes (morphine-like agonists)**				
	Codeine (various)	+++	200mg	0.15	-Avoid daily doses >600mg po; -Not for use in children under 12 yo
	Synthetic opioid				
	Tramadol (Tramacet= 37.5mg Tramadol + 325mg APAP- max 8 tabs per day)	N/A	N/A	100mg ≈10-20mg po morphine	Not recommended: <18yr or if seizure/suicide hx Low affinity for mu; also ↑serotonin & noradrenaline, Metabolized to active metabolite by

Commonly Prescribed NSAIDs for acute Pain

Drug	Class	Dose	Comment	General
Ibuprofen ADVIL, MOTRIN	PROPIONIC ACIDS	Lowest Anti-inflammatory: 400-600mg po TID Analgesic ceiling at 400mg Usual: 200-800mg po TID-QID; Max: 2.4-3.2g/d	most favourable benefit–risk profile of all NSAIDS	ASA → give NSAID 30min after or 8hrs before immediate release ASA. Max labeled dose for OTC NSAIDs lower than Rx for safety Suppository formulation are not safer for GI tract
Naproxen NAPROSYN	PROPIONIC ACIDS	Lowest Anti-inflammatory: 375mg po BID Usual Range: 125-500mg po BID; Max:1.5g/day ALEVE 220mg po BID-TID; Max: 440mg/day	Naproxen Na+ ANAPROX: faster acting	
Diclofenac Sodium VOLTAREN	PHENYLACETIC ACIDS	Lowest Anti-inflammatory: 50mg po BID 75-100mg SR po daily Usual: 25-50mg po BID-TID **Max: 100mg/day**	Topical route available May ↑LFTs AST >4%	
Ketorolac TORADOL,	PYROLIZINE CARBOXYLIC ACID	Lowest Anti-inflammatory: 10mg po QID Usual (po): 10mg QID x7d max; Max: 40mg/d	Only NSAID available via injection (IM/PO)	
Celecoxib CELEBREX	COX-2 Inhibitor	Lowest Anti-inflammatory: 200mg po daily-BID Usual: AS/OA: 100mg po BID, RA: 200mg po BID	Equal efficacy compared to other NSAIDs AE: rare SULPHA allergic type	Minimal GI mucosal effect; comparable dyspepsia to NSAIDS