

Advances in Dental Pain Management

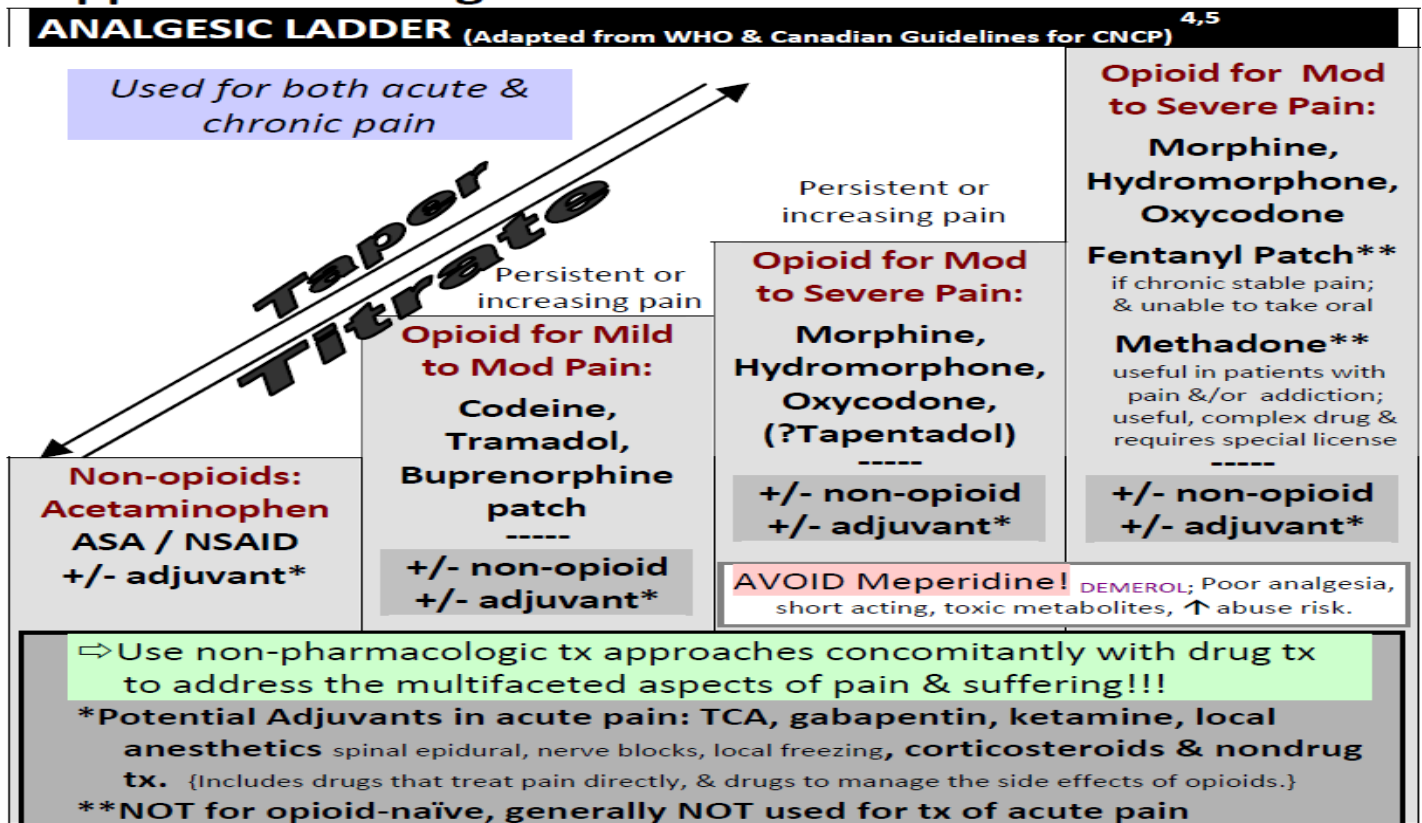
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I. AMBULATORY DENTAL PAIN CONTROL STRATEGY

Pain Control Strategy		
	NSAIDs Indicated (Patients who Can take ASA-like Drugs)	NSAIDs CONTRA Indicated (Patients who Can't take ASA-like Drugs)
Mild Pain	<u>Ibu 200 mg-400mg scheduled four times a day</u>	<u>APAP 650 – 1000 mg up to 4000mg per day</u>
Moderate Pain	<u>NSAID – Up to maximum Effective Dose</u>	<u>APAP 650 – 1000 mg With equivalent of Hydrocodone 5-10mg scheduled four times a day</u>
	<u>NSAID Plus APAP Or NSAID Plus APAP/HC.</u>	
Severe Pain	<u>NSAID – Max Dose and APAP/Oxycodone 10 mg Combination</u>	<u>Acetaminophen 1000 mg with equivalent of Oxycodone 10 mg scheduled four times a day</u>

II. WHO ANALGESIC LADDER RELATES TO CANCER PAIN

Approach to Drug Tx in Pain



CNCP=chronic non-cancer pain CP = Chronic Pain ER MD=emergency physician fx=function FP=family physic PIP=Prescription Information Program (SK) **Exit Strategy:** developed in concordance with physicians in Saskat

Dose-Response for Three Types of Oral Analgesics

- Opioids provide unlimited pain relief but side effects and abuse potential limit their use in ambulatory patients
- Ibuprofen and equi-analgesic oral doses of other NSAIDs provide a ceiling analgesic effect. Increasing beyond ibuprofen 400mg DOES increase anti-inflammatory effect which is an essential component of acute dental pain.
- ASA/APAP provide a lower ceiling analgesic effect which reaches maximum analgesic at 1000mg.
- APAP combined with NSAIDs shows a synergistic effect on acute dental pain and these two agents should be dosed concomitantly to maximize non-opioid pain control for acute dental pain.

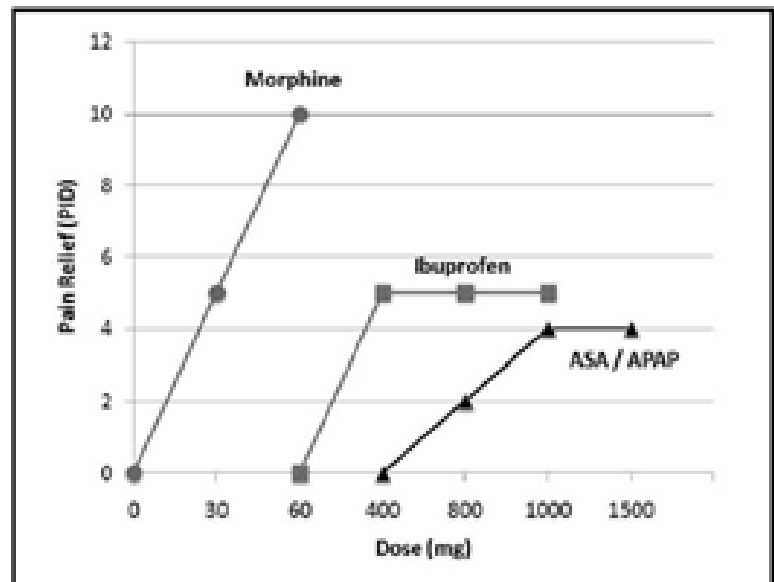


Figure 2. Analgesic efficacy. This graph illustrates a typical dose-response curve for orally administered (PO) analgesics. The dose-response curve for opioids such as morphine demonstrates unlimited efficacy in which greater doses provide greater analgesia. At equipotent doses, all opioids demonstrate a similar dose response. In contrast, nonopioids demonstrate a “ceiling” effect that generally is adequate for relief of mild to moderate pain (pain relief rating of 4–5 in this scale). For ibuprofen, doses greater than 400 mg do not provide further analgesia. For aspirin (ASA) and acetaminophen (APAP), this ceiling effect is achieved at 1000 mg and is somewhat lower than that provided by nonsteroidal anti-inflammatory drugs (NSAIDs).

III. ACETAMINOPHEN (APAP, Tylenol, g)

Maximum daily dosage:

- *ACUTE THERAPY:* Maximum of 4 g/day monitored and 3g/day unmonitored
- *CHRONIC THERAPY +/or ELDERLY PATIENT:* Maximum of 2.6 grams APAP/day

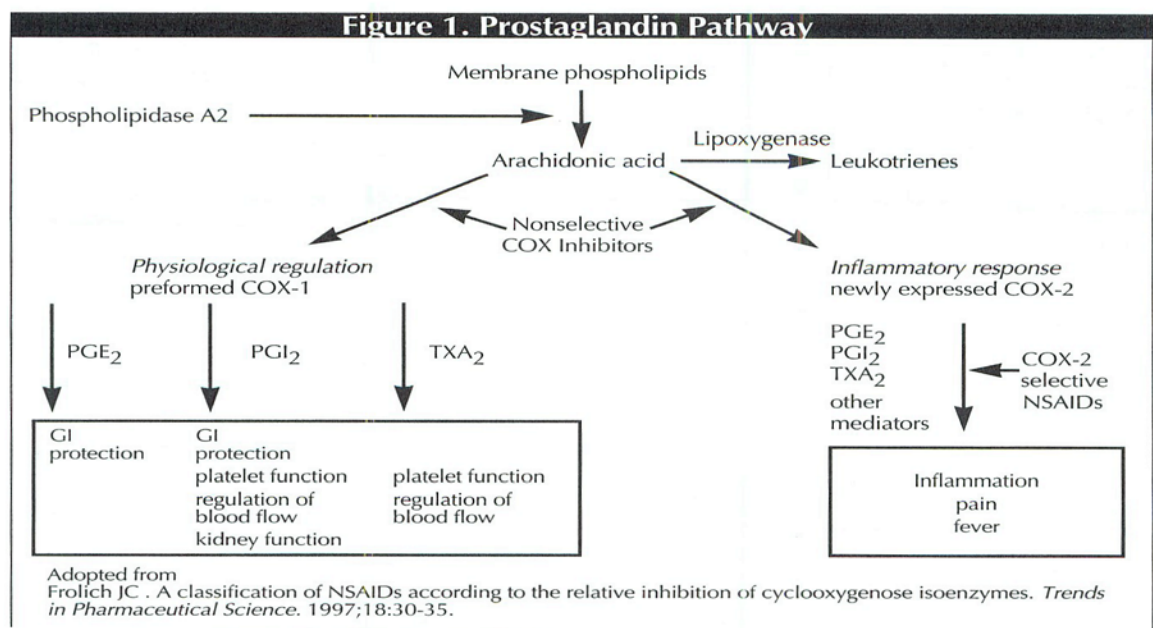
<u>PRODUCT</u>	<u>DOSAGE</u>	<u>ACUTE</u>	<u>CHRONIC</u>
Regular Strength APAP	325mg	12/day	8/day
Extra Strength APAP	500mg	8/day	5/day
Extended Relief APAP	650mg	6/day	4/day

Toxicity risk is increased by:

- *Fasting during acetaminophen therapy*
- *3 or more alcoholic drinks per day*

TOXICITY: ORAL: Ingestions of 200 mg/kg or 10 g, whichever is less, are considered potentially toxic. **IV:** A 10 fold overdose caused hepatotoxicity in a chronically malnourished child. **THERAPEUTIC DOSE: ADULT: Oral:** 650 to 1000 mg every 4 hours up to 4 g/day. **IV: (50 kg or greater):** 650 to 1000 mg every 4 to 6 hours, up to 4 g/day; (less than 50 kg): 12.5 mg/kg to 15 mg/kg every 4 to 6 hours, up to 3750 mg/day (75 mg/kg/day). **PEDIATRIC: Oral:** 10 to 15 mg/kg every 4 hours up to 60 mg/kg/day. **IV:** 12.5 mg/kg to 15 mg/kg every 4 to 6 hours, up to 75 mg/kg/day.

IV. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (Non-acetylated)



A. NSAIDS COMMONLY USED FOR ACUTE PAIN AND INFLAMMATION

NSAID	ROLE in Therapy *	T_p (hr)	t 1/2 (hr)	ANALGESIC Onset (hr)	DURATION (hr)	USUAL ADULT DOSE (mg)	MAX. DAILY DOSE (mg)
<u>PROPRIONIC ACIDS</u>							
<i>flurbiprofen (Ansaid G)</i>	P	1.5	5.7	2	6-7	50-100 q4-6h	300
<i>ibuprofen (Motrin, G, etc)</i>	P	1-2	1.8-2.	.5	4-6	400-600 q4-6h	3200/1200
<i>ketoprofen (Orudis, OTC, G)</i>	P,I	.5-2	2-4	1	6-7	50 q6-8h	300/75
<i>naproxen (Naprosyn, G)</i>	P,I	2-4	12-15	1	up to 7	500 stat, then 250 q6-8h	1500
<i>naproxen Na (Anaprox, DS, G)</i>	P,I	1-2	12-13	1	up to 7	550 stat, then 275 q6-8h	1650
<i>naproxen Na (Aleve - OTC, G)</i>	P,I	1-2	12-13	1	up to 7	440 stat, then 220 q 8-12h	660
<u>ACETIC ACIDS</u>							
<i>diclofenac K (Cataflam)</i>	P,I	1-2	1-2	.5	4-6	100 stat, then 50 q6-8h	200
<i>diclofenac Na (Voltaren, G)</i>	P,I	2-3	1-2	1	4-6	50 q6h	200
<i>etodolac (Lodine, G)</i>	P	1-2	7.3	.5	4-12	200-400 q6-8h	1200
<i>ketorolac (Toradol oral, G)</i>	P	.5-1	3.8-6	.5	6-8	20 stat, then 10 q4-6h	40
<i>nabumetone (Relafen, G)</i>	P,I	2-4	24	4	up to 12	750-1000mg q 12h	2000
<u>SALICYLATE</u>							
<i>diflunisal (Dolobid, G)</i>	P,I	2-3	8-12	1	8	1000 stat, then 500 q8h	1500
<u>COX-2 SELECTIVE</u>							
<i>Celecoxib (Celebrex)</i>	I	3	11	2	up to 24h	100-200mg 1d-bid	400

*P=pain relief, I=inflammation reduction

B. CLINICAL APPLICATIONS:

1. NSAIDS VS OPIOIDS

ADVANTAGES OF PRESCRIBING NSAIDS

no sedation, constipation or respiratory depression
reduced swelling and trismus
no central nausea and vomiting side effects
no potential for abuse or habituation

DISADVANTAGES OF NSAIDS

GI irritation is common
no adult liquid preps are available
patient expectations are not fulfilled
no activity limitations or sedation
possible increased risk of blood clots

2. GENERAL PRESCRIBING GUIDELINES

- a) NSAIDS can be mixed with narcotics +/- acetaminophen for additional effects, not synergistic
- b) AVOID NSAID + NSAID combinations:
 - take medication history, including OTC agents
 - no therapeutic advantage, deleterious effects on GI tract, platelets
- c) NSAID failure - try switching chemical classes
 - acetic acid derivatives are structurally different so switching may improve response

3. PATIENT-SPECIFIC FACTORS

<i>AERD (Samter's Triad)</i>	Asthma, chronic urticaria, nasal polyps = sensitivity triad.
<i>ASTHMA</i>	Avoid NSAIDS if one triggers asthma, avoid COX-2s
<i>ELDERLY</i>	Choose NSAID with short t _{1/2} to avoid accumulation
<i>GASTRITIS, ALCOHOLISM</i>	Use cytoprotective agent prophylaxis, COX-2s are better
<i>LIVER DISEASE</i>	Avoid diclofenac and piroxicam (Feldene)
<i>HIATAL HERNIA</i>	AVOID ASPIRIN, caution with any NSAID, COX-2s are better
<i>PEPTIC ULCER HX</i>	Caution with any agent, may need prophylaxis, COX-2s are better
<i>POST-OP PAIN</i>	Ketorolac very effective if substance abuse history
<i>RENAL DISEASE</i>	Caution, diflunisal may be best NSAID, COX-2s NO BETTER
<i>MAJOR SURGERY</i>	D/C ASA 1 week prior, D/C other NSAIDS 24 hours prior, Celebrex DOESN'T increase bleeding risk and don't have to be D/C'd.
<i>CLOPIDOGREL THERAPY</i>	CONSIDER AVOIDING NSAID THERAPY INCLUDING CELECOXIB
<i>ANTICOAGULANT THERAPY</i>	AVOID NSAID THERAPY. COX-2's increase bleeding due to a drug intx.

C. INDIVIDUAL AGENTS

1. IBUPROFEN (*Motrin, g*)

- Many dosage forms: 100mg caplet, 50 & 100mg chewable tablets, 100mg/5ml susp, gel caps
- still the best first line agent due to good safety profile and reliable efficacy in acute pain (Oxford League)
- 800mg q 6 hours can be given initially, no anti-inflammatory value in doses above 3200mg/day

2. NAPROXEN SODIUM (*Anaprox, Anaprox DS, G*)

- May give lowest risk of blood clots so safest for atherosclerosis or peripheral artery disease
- Longer half-life than ibuprofen so may accumulate in elderly but works for about 8 hours

3. KETOROLAC (*Toradol, g, Sprix Nasal Spray*)

MANUFACTURER PRESCRIBING GUIDELINES LIMIT USE OF ORAL TABLETS

- Prescribing guidelines limit tablet use in response to serious adverse events
- Manufacturer bears less responsibility for adverse outcomes if practitioner uses medication outside of labeling
- Emphasizes the importance of proper patient selection criteria for all NSAIDS

V. TRAMADOL (Ultram, G, Ultracet - Ortho/McNeil, RYBIX ODT - Victory)

A. MECHANISM OF ACTION:

- unique complimentary dual mechanisms
- tramadol is a weak opioid receptor binder as well as an inhibitor of serotonin and norepinephrine reuptake
- no inhibition of prostaglandin synthesis
- **controlled substance Schedule IV as of 8/18/14/ FDA pregnancy category C**

B. THERAPEUTIC USE: 100MG =ASA/codeine 650/60 for acute pain.

COMBINATION: Ultracet = 37.5mg tramadol/325mg acetaminophen, Ultram ER

C. ADVERSE REACTIONS:

Dizziness	26%	Nausea	24%
Constipation	24%	Headache	18%
Sedation	16%		

D. DRUG INTERACTIONS

carbamazepine → → reduced tramadol effectiveness

MAOI → → possible sympathomimetic potentiation (AVOID TRAMADOL)

CYP206 inhibitor → → increased tramadol levels – caution with Prozac, Paxil, Zoloft SSRIs

CNS depressants → → increased tramadol sedation

E. DOSAGE & ADMINISTRATION

- 50-100mg q 4-6 hours prn pain to maximum of 400mg/day (max dose for pts > 75 years is 300mg/day)
- 100mg initially is more effective for severe pain
- Tramadol 50mg ODT (Rybix) gives faster onset and comes in a 50mg tablet with no generic

F. PATIENT SELECTION CRITERIA

- Patients on NSAIDs, Warfarin, Pradaxa, Eliquis, Xarelto, Savaysa or oral hypoglycemics
- Patients with history of histamine release with opiates or on hemodialysis
- Diagnosis of neuropathic pain or history of gastrointestinal ulceration
- **Patients with an opiate dependence hx. Should not take tramadol – Controlled Substance Schedule IV**
- **Patients with severe allergic rx to CODEINE OR OTHER OPIATES should NOT take tramadol**

VI. Corticosteroids for Dental Pain and Inflammation Management

Glucocorticoid	Approximate equivalent dose (mg)	Relative anti-inflammatory (glucocorticoid) potency	Relative mineralocorticoid potency	Half-life	
				Plasma (min)	Biologic (hrs)
<i>Short-acting</i>					
Cortisone	25	0.8	2	30	8-12
Hydrocortisone	20	1	2	80-118	8-12
<i>Intermediate-acting</i>					
Prednisone	5	4	1	60	18-36
Prednisolone	5	4	1	115-212	18-36
Triamcinolone	4	5	0	200+	18-36
Methylprednisolone	4	5	0	78-188	18-36
<i>Long-acting</i>					
Dexamethasone	0.75	20-30	0	110-210	36-54
Betamethasone	0.6-0.75	20-30	0	300+	36-54

- 25 high quality studies in post extraction patients show effectiveness for pain, trismus and swelling thereby reducing need or demand for opiates
- 15 high quality studies in patients post RCT show effectiveness in reducing pain, swelling and inflammation thereby reducing need for opiates
- Opioid-sparing analgesia is what we are striving for in dentistry
- Contra-indications:
 - Uncontrolled diabetics or Type I Diabetics
 - Severe psychiatric conditions
 - Angle-closure glaucoma
 - Pediatric or pregnant patients

VII. OPIOID ANALGESICS

A. OPIOIDS COMMONLY USED ORALLY FOR MILD TO MODERATE PAIN

OPIOID AVAILABLE	EQUIANALG. DOSE (MG)	PEAK (HR)	DURATION (HR)	COMMENTS	PRECAUTIONS
Codeine (avoid in pts. On 2D ₆ inhibitors* - Prozac, Paxil, Cymbalta)	50	1.5-2	4-6	2D ₆ polymorphism may cause toxicity-not for pediatric patients	Impaired ventilation, asthma, high intracranial pressure
Hydrocodone (Vicodin-ES,HP, Lortab,Zydone,G)	7.5	2	4-6	not useful after 10mg q 3 hr	Most addictive Schedule 3 Health care providers are at risk of abuse
Meperidine (Demerol,G)	75	1-1.5	4-5	Biotransformed to normeperidine, a toxic metabolite, max dose 200mg/24 hours orally	Normeperidine can accumulate with repeated dosing – causing seizures, avoid in pts. on MAOIs
Oxycodone (Percodan, Percocet,G)	5	1	3-4	not useful after 10mg q 3 hr	always a C II substance as it causes euphoria
Tramadol (avoid in pts. On 2D ₆ inhibitors*)	75			2D ₆ polymorphism may cause toxicity-not for peds	Schedule IV CS

*Amiodarone, Cimetidine, Desipramine, Duloxetine, Fluoxetine, Paroxetine, Propafenone, Quinidine, Ritonavir

B. CLINICAL USE OF NARCOTIC ANALGESICS

1. POTENCY ESCALATION

STEP 1. Maximize non opioids

STEP 2. Add Opioids for “rescue”

STEP 3. Increase Opioid potency if needed

Rx: Hydrocodone 5mg w/APAP 325mg (Lorcet,G)
Disp: #8 (5mg of Hydrocodone = 50mg of Tramadol)
Sig: 1 tab q 6 hrs prn pain. Take with food/milk

Rx: Oxycodone 5mg w/APAP 325mg (Percocet, G)
Disp: #6 (5mg of Oxy = 7.5mg of Hydrocodone)
Sig: 1 tab q 6 hrs prn pain. Take with food/milk

PATIENT CAUTIONS/INSTRUCTIONS

STEP 1. Combine NSAID&APAP for **SYNERGISM**

STEP 2. Add opioids for additional pain relief or rest

STEP 3. Increase potency only if uncomfortable at rest
 - if vestibular or GI problems, try 1/2 dose with 1/2 dosing interval

to provide **ADDITIVE** pain relief & for sleep/anxiety
 - consider APAP content of RX when prescribing

-hydrocodone/APAP is Schedule II as of 10/6/14

-oxycodone/APAP has always been Schedule II

NOTE: Percocet now comes in FOUR combinations (2.5/325, 5/325, 7.5/325, 10/325)

C. FIXED OPIOID COMBINATIONS WITH IBUPROFEN – useful for APAP allergic patients

1. OXYCODONE 5MG/IBUPROFEN 400MG (COMBUNOX)
2. HYDROCODONE 2,5, 5.0,7.5mg or 10mg/IBUPROFEN 200mg (VICOPROFEN,g)

D. ALLERGY VS PSEUDO-ALLERGY

True allergies involve an immune response while other reactions can fall into either side effects or pseudoallergy, which is generally the result of histamine release but no actual immune response. Below are some groups of symptoms followed with points to take into consideration when a patient exhibits one or more of the symptoms.

If the following symptoms occur with respect to opioid administration, they are likely related to a pseudoallergy rather than a true IgE mediated drug allergy:

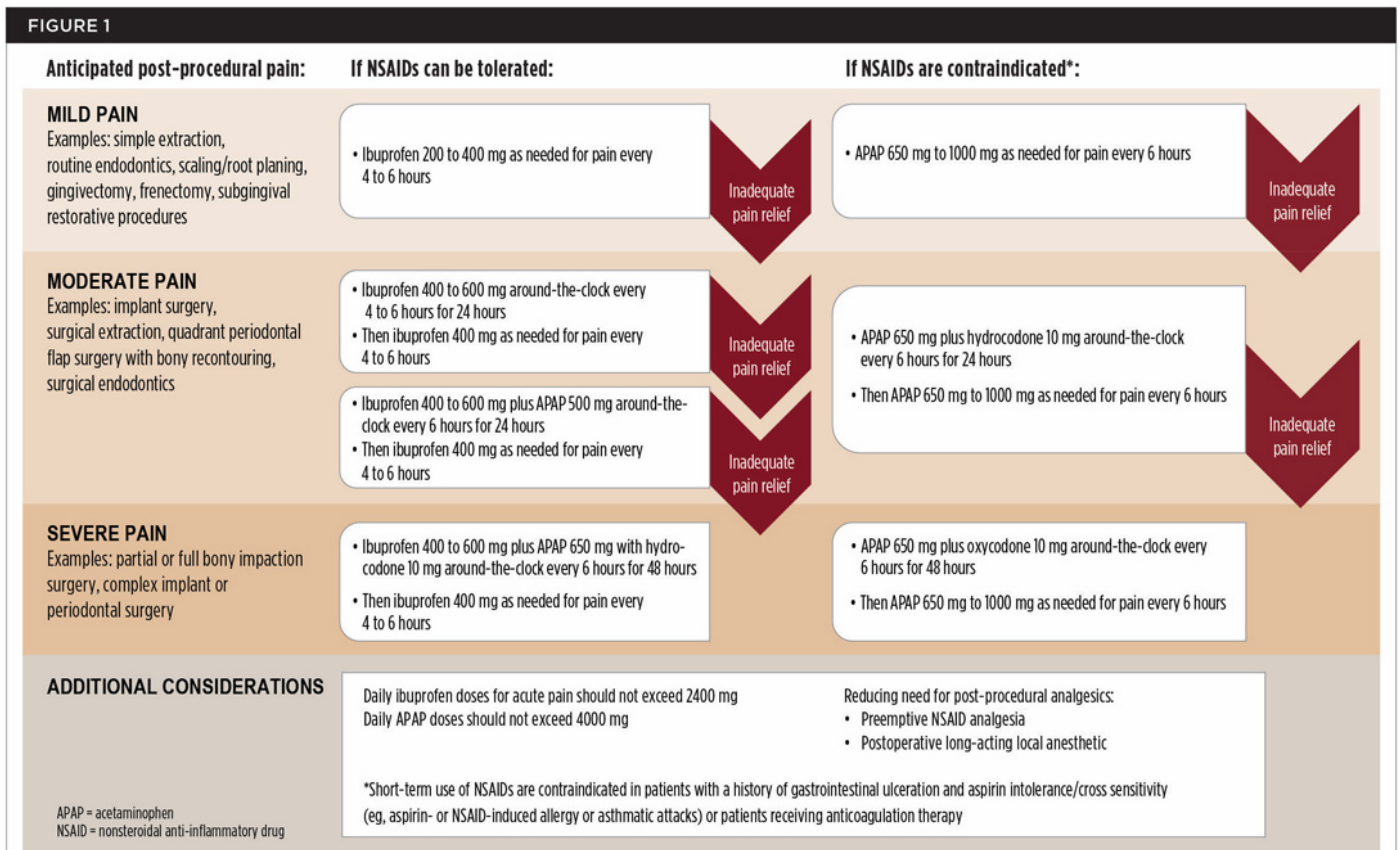
- ✓ Generalized flushing, itching, sweating
- ✓ Mild hypotension accompanied by nausea and/or vomiting
- ✓ Itching, flushing, or hives at injection/application site

Pseudoallergy reactions can be managed and/or minimized using the following strategies:

- ▶ Try nonopioid analgesic if mild pain (acetaminophen & NSAID given at the same time)
- ▶ Avoid codeine, morphine & meperidine as these are most likely to trigger pseudoallergy.
- ▶ Use a more potent opioid (drugs listed below from least to most potent):
- ▶ Meperidine < codeine < morphine < hydrocodone < oxycodone < hydromorphone < fentanyl
- ▶ If effective against pain and symptoms are mild, consider administering opioid with an antihistamine such as diphenhydramine 25mg preferably in liquid form 30min prior to opioid dose.
- ▶ Consider reduction in opioid dose with more frequent administration if tolerated.

E. Prescribing Analgesics for Postoperative Dental Pain *Compendium of Continuing Education in Dentistry*

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PEDIATRIC ANALGESIC DOSAGES FOR DENTAL PAIN

	ONSET (min)	PEAK (hrs)	DURATION (hrs)	PEDIATRIC DOSE (mg/day)	AVAILABLE PEDIATRIC PREPARATIONS
<u>Non-Narcotics</u>					
Acetaminophen (Tylenol, Tempra, Panadol, g.)	20-30	0.5-2	3-7	10mg/kg q 4-6 hrs (max 65mg/kg/day)	Oral Solution: 48-325mg/5ml Chewable tabs: 80 + 160mg Rectal supp: 120,125,325,650mg
Diclofenac (Voltaren -Na ⁺ salt) (Cataflam- K ⁺ salt)	120 30	3 1	4-6 4-6	2-4mg/kg/day (max 200mg/day)	Diclofenac EC tab 25, 50, 75mg Cataflam tab 50mg
Diflunisal (Dolobid, g)	60	2-3	4-7	10mg/kg q 8 hrs (max 1500mg/day)	Tablets:250, 500mg
Ibuprofen (Advil, Children's Motrin, Medipren, Nuprin, g)	20-30	1-2	4-6	5-10mg/kg q4-6 hrs (max 40mg/kg/day)	Oral Susp: 100mg/5ml Chew tabs: 50, 100mg Caplet:100 ,200mg Tablets: 200,400,600,800mg
Ketoprofen (Orudis, Oruvail, g) OTC-Actron, Orudis KT	30	1-2	4-6	0.5-1mg/kg q6-8 hrs (max 300mg/day)	Capsules: 25,50,75mg Ext.Release (Oruvail) 200mg
Naproxen (Naprosyn, g)	60	1-2	4-7	10mg/kg/day (max 1500mg/day)	Oral Susp: 125mg/5ml Tablets: 250,375,500mg
Naproxen Na (Anaprox, DS, g)	60	1-2	4-7	11 mg/kg/day (max 1650mg/day)	Tablets: 220,275, 500mg Caplets: 220mg
<u>Narcotics</u>					
Codeine (sulfate or phosphate) (ultra-fast metabolizers can suffer toxic effects)-BLACK BOX WARNING in children post tonsillectomy and/or adenoidectomy. DON'T USE.	15-30	0.5-1	3-6	0.5mg/kg q4 hr (max120mg/day)	Codeine PO ₄ /promethazine oral syrup: 10mg +6.25mg/5ml Codeine/APAP elixir: 12mg/120mg per 5ml susp: 12mg/120mg/5ml
Hydrocodone (Hydrocet, Lorcet, Vicodin, Zydone, g) FDA issued Drug Safety Communication 1/11/18 stating that no one under age 18 years should receive codeine, hydrocodone or tramadol for cough/cold. DON'T USE.	15-30	0.5-1	4-8	0.1-0.2mg/kg q4-6h (max= 90mg/day)	Lortab Elixir: 2.5 HC + 167 APAP/5ml Tabs: 5/325 (Lorcet,g) 2.5/325 (Lortab) 7.5/325 (Lortab 7.5)
Meperidine (Demerol, g) (Safe choice for patient allergic to morphine/codeine group)	15-45	1	4-5	1-3mg/kg q 3-4h (max 20mg/kg/day)	Tabs: 50,100mg Oral Soln: 50mg/5ml Mepergan Fortis: 50mg MPD/ 25mg promethazine