USEFUL DRUG & DENTAL MANAGEMENT REFERENCES

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I. PROPERTIES OF THE IDEAL DRUG REFERENCE

- **Comprehensive** - index lists brand and generic names of all drugs marketed in country of choice
- **Comparative** - includes tables of drug categories vs. side effects, kinetics, interactions, spectrum of action for antimicrobials and clinical characteristics for analgesics
- **Complete** - includes both prescription AND OTC medications in U.S. and Canada

II. GENERAL DRUG REFERENCE SOURCES

A. LEXI-COMP DRUG INFORMATION HANDBOOK FOR DENTISTRY – www.lexi.com
-2025 Handbook 30th ed. Final edition is $114.95, available for one or more office PCs as well
-UPTODATE Lexidrug Dental Mobile Pro Package is $199/year and includes Lexi-Interact
PDA/Android,iPhone,iPad,iTouch,,HP,PocketPC,PalmOS:**Dental Lexi Drugs is $75/year**

B. EPOCRATES (free) AND EPOCRATES RX PRO ($175/year) are useful in dental practice

C. DRUGS.COM and MEDSCAPE can supplement your online drug-related info at no charge

D. MOSBY'S DENTAL DRUG REFERENCE, 14th edition published November 2024 costs $58.39

III. SPECIFIC DENTAL DRUG RESOURCES

A. GUIDE TO ANTIMICROBIAL THERAPY 2024 (June every year) – www.sanfordguide.com
-desktop, spiral bound, softcover, PDA/Pocket PC versions available
-Spiral is $45.00, softcover is $35.00, don't buy on Amazon – use the Sanford Guide website

B. PEDIATRIC DRUG DOSAGE HANDBOOKS

1. Harriet Lane Handbook: 23rd Edition. $ 58.49 Mosby. May 2023 (published every 3 years)
2. Pediatric Lexi-Drugs for Blackberry by Lexi-Comp
3. LexiComp Pediatric & Neonatal Dosage Handbook 25th edition, $109.952023-2024

C. ANXIOLYSIS AND CONSCIOUS SEDATION HANDBOOKS

1. **Malamed Stanley. Sedation: A Guide to Patient Management. 7th edition, 2025, Elsevier Health Sciences ($107.99) and available 9/01/2025**
2. **Handbook of Nitrous Oxide and Oxygen Sedation. 6th edition, April 14, 2025 Mosby ($73.99)**

D. DENTAL MANAGEMENT GUIDES

1. **Malamed Stanley. Medical Emergencies in the Dental Office. 8th edition. 2022 (89.95)**
2. **Little and Falace. Dental Management of the Medically Compromised Patient. 10th edition. May 2023 (book-106.99, ebook – 86.95)**
3. **Malamed Stanley. Handbook of Local Anesthesia. 7th edition, June 2019.**
4. **Dym, Harry. Clinical Pharmacology for the Oral and Maxillofacial Surgeon.1st ed. 2022**

IV. Herbal and Nutritional Drug Product References

A. Natural Medicines TRC Healthcare – www.naturalmedicines.therapeuticresearch.com
-best resource for health professionals and very detailed for $19/month.

B. Nutrition Action Health Letter – www.cspinet.org
-published by Center for Science in the Public Interest (CSPI) - $24/10 issues per year or $58 for 3 years

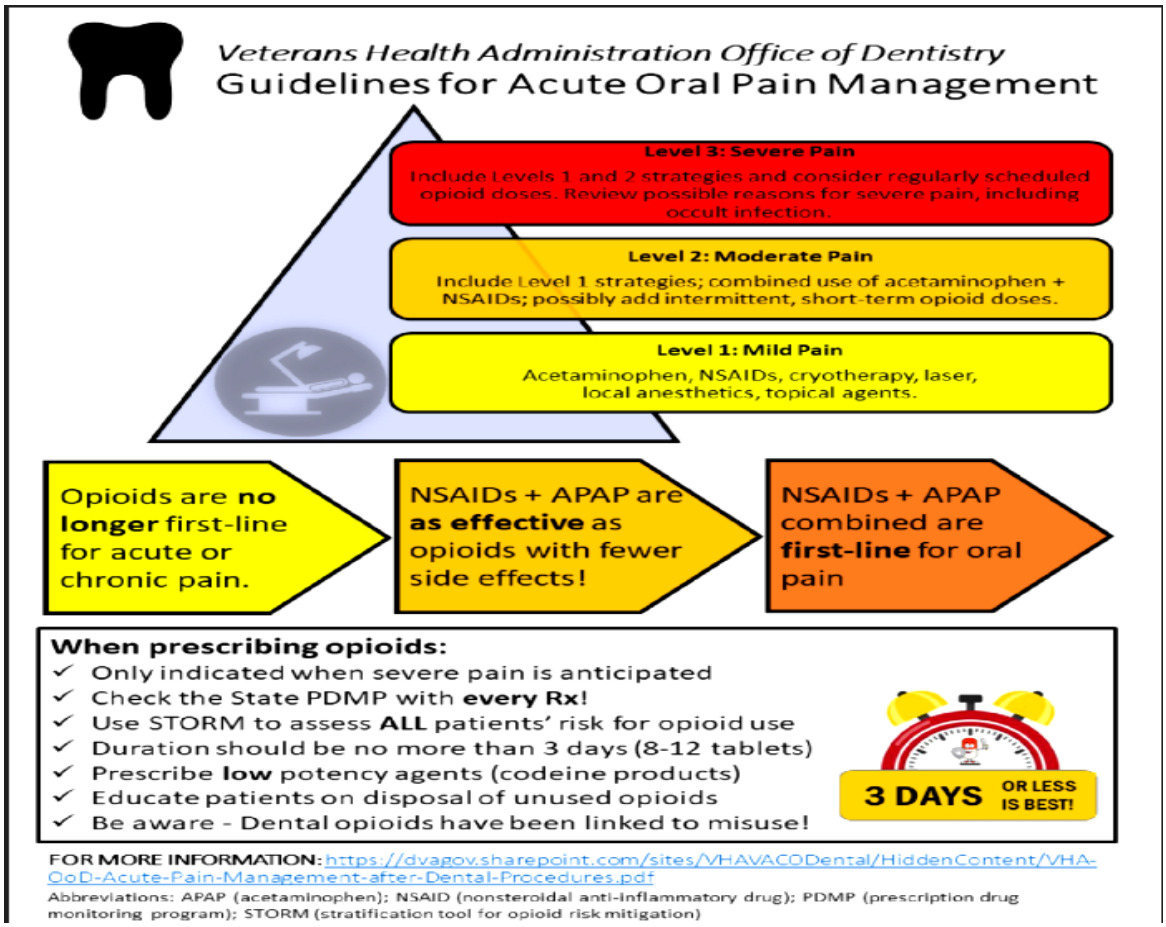
C. Other Useful Websites
-**www.consumerlab.com**-excellent resource & $45/year, www.quackwatch.com, naturowatch.com
-www.science-basedmedicine.org. www.supplement-clarity.com with author Joe Cannon, M.S.

Advances in Dental Pain Management

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	Ibu 200 mg-400mg scheduled four times a day	APAP 650 – 1000 mg up to 4000mg per day
Moderate Pain	NSAID – Up to maximum Effective Dose	APAP 650 – 1000 mg With equivalent of Hydrocodone 5-10mg scheduled four times a day
	NSAID Plus APAP Or NSAID Plus APAP/HC.	
Severe Pain	NSAID – Max Dose and APAP/Oxycodone 10 mg Combination	Acetaminophen 1000 mg with equivalent of Oxycodone 10 mg scheduled four times a day

II. VETERANS HEALTH ADMINISTRATION OFFICE OF DENTISTRY



Anesth Prog. 2010 Summer;57(2):67–79. doi: 10.2344/0003-3006-57.2.67

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-opoid pain control for acute dental pain.

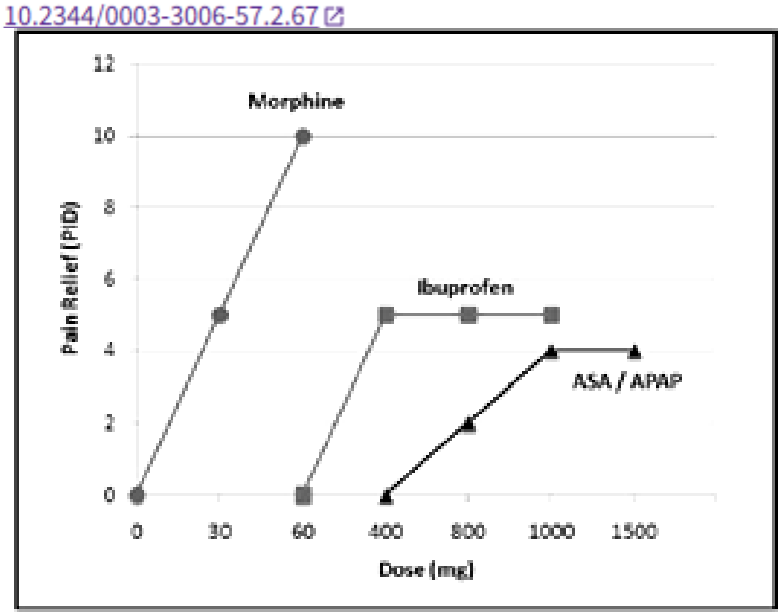


Figure 2. Analgesic efficacy. This graph illustrates a typical dose-response curve for orally administered (PO) analgesics. The dose-response curve for opioids such as morphine demonstrates unlimited efficacy in which greater doses provide greater analgesia. At equipotent doses, all opioids demonstrate 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

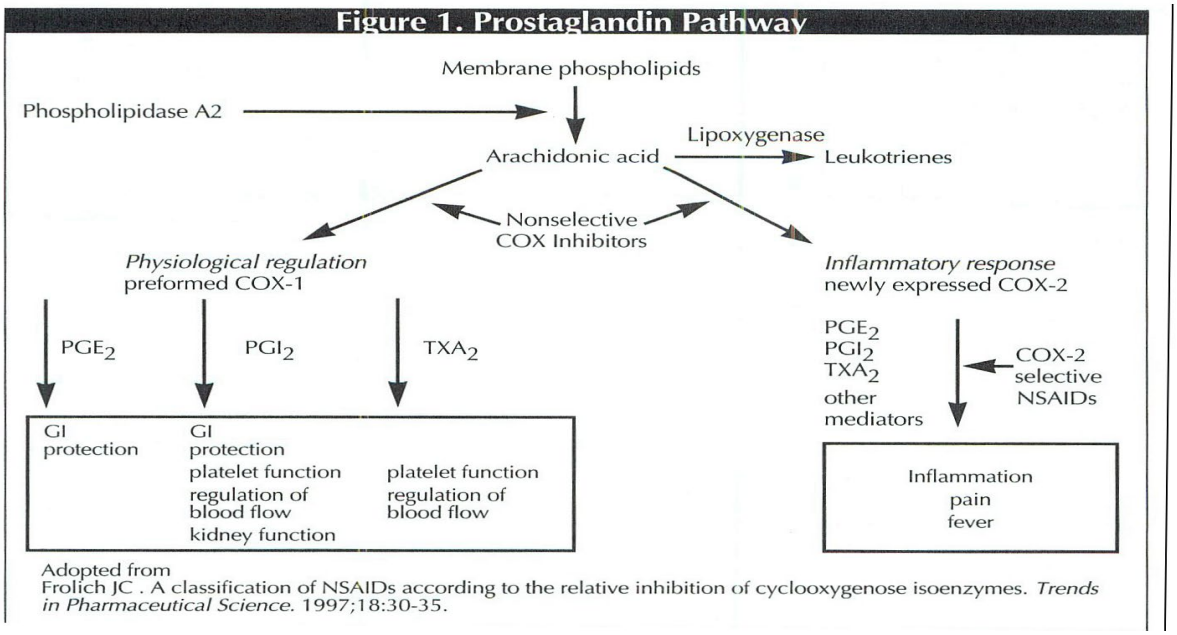
PRODUCT	***DOSAGE***	***ACUTE***	***CHRONIC***
Regular Strength APAP	325mg	12/day	8/day
Extra Strength APAP	500mg	8/day	5/day
Extended Relief APAP	650mg	6/day	4/day

Toxicity risk is increased by:

- *Fasting (depleted glutathione) and/or dehydration during acetaminophen therapy*
- *Greater than two 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 **	*Tp (hr)*	*t 1/2 (hr)*	*ANALGESIC Onset (hr)*	*Duration (hr)*	*USUAL ADULT DOSE (mg)*	*MAX. DAILY DOSE (mg)*
PROPRIONIC ACIDS							
ibuprofen (Motrin,G,otc)	P	1-2	1.8-2.	.5	4-6	400-600 q4-6h	3200/1200
naproxen(Naprosyn,G)	P,I	2-4	12-15	1	up to 7	500 stat, then 250 q6-8h	1500
naproxen Na (Anaprox,DS,G)	P,I	1-2	12-13	1	up to 7	550 stat, then 275 q6-8h	1650
naproxen Na (Aleve – OTC,G)	P,I	1-2	12-13	1	up to 7	440 stat, then 220 q 8-12h	660
ACETIC ACIDS							
diclofenac K(Cataflam)	P,I	1-2	1-2	.5	4-6	100 stat, then 50 q6-8h	200
diclofenac Na (Voltaren,G)	P,I	2-3	1-2	1	4-6	50 q6h	200
etodolac (Lodine,G)	P	1-2	7.3	.5	4-12	200-400 q6-8h	1200
ketorolac (Toradol oral,G)	P	.5-1	3.8-6	.5	6-8	20 stat, then 10 q4-6h	40
nabumetone (Relafen,G)	P,I	2-4	24	4 2	up to 12	750-1000mg q 12h	2000
ENOLIC ACIDS							
Meloxicam (Mobic,G)	P	5	20-26	4	up to 24	5-15mg once daily	15
Piroxicam (Feldene,G)	P	5	50	4	up to 48	10-20mg once daily	20
SALICYLATE							
diflunisal (Dolobid,G)	P,I	2-3	8-12	1	8-12	1000 stat, then 500 q8h	1500
COX-2 SELECTIVE							
Celecoxib (Celebrex)	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	*DISADVANTAGES OF NSAIDS*
no sedation, constipation or respiratory depression	GI irritation is common
reduced swelling and trismus	no adult liquid preps are available
no central nausea and vomiting side effects	patient expectations are not fufilled
no potential for abuse or habituation	no activity limitations or sedation
	possible increased risk of blood clots

2. GENERAL PRESCRIBING GUIDELINES

a) NSAIDS can be mixed with narcotics +/or 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
-pre procedural dosing of ibuprofen 400mg or naproxen sodium 275mg reduces postop pain

3. PATIENT-SPECIFIC FACTORS

AERD (Samter's Triad)	Asthma, chronic urticaria, nasal polyps = sensitivity triad.
ASTHMA	Avoid NSAIDS if one triggers asthma, avoid COX-2s
ELDERLY	Choose NSAID with short t ½ to avoid accumulation
GASTRITIS, ALCOHOLISM	Use cytoprotective agent prophylaxis, COX-2s are better
LIVER DISEASE	Avoid diclofenac and piroxicam (Feldene)
HIATAL HERNIA	AVOID ASPIRIN, caution with any NSAID, COX-2s are better
PEPTIC ULCER HX	Caution with any agent, may need prophylaxis, COX-2s are better
POST-OP PAIN	Ketorolac very effective if substance abuse history
RENAL DISEASE	Caution, diflunisal may be best NSAID, COX-2s NO BETTER
MAJOR SURGERY	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.
CLOPIDOGREL THERAPY	CONSIDER AVOIDING NSAID THERAPY INCLUDING CELECOXIB
ANTICOAGULANT THERAPY	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 serve to limit tablet prescribing 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 (G, Conzip, ER in 100, 200, 300mg))

A. MECHANISM OF ACTION:

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

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

C. ADVERSE REACTIONS:

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

D. DRUG INTERACTIONS

carbamazepine $\rightarrow\rightarrow$ reduced tramadol effectiveness
MAOI $\rightarrow\rightarrow$ possible sympathomimetic potentiation (AVOID TRAMADOL)
CYP206 inhibitor $\rightarrow\rightarrow$ increased tramadol levels – caution with Prozac, Paxil, Zoloft SSRIs
CNS depressants $\rightarrow\rightarrow$ 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

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 <u>not</u> take tramadol – Controlled Substance Schedule IV**
- **Patients with severe allergic rx to CODEINE OR OTHER OPIATES should NOT take tramadol**

VI. SUZETRIGINE (Journavx)-novel peripheral sodium ion channel blocker

A. MECHANISM OF ACTION:non-opioid highly selective inhibitor of voltage-gated sodium ion channel Nav1.8.
B. Rx: Journavx 50mg tabs, Disp: #7 Sig: 2 tabs initially, then one tab every 12 hours for up to five days. Cost = $120
C. ADVERSE EFFECTS: nausea, headache, constipation, dizziness, vomiting. Headaches are mild and last one day.
D. Efficacy in abdominoplasty & bunionectomy is equivalent to hydrocodone with acetaminophen.
E. PATIENT SELECTION CRITERIA-use if opioids and/or NSAIDs are contraindicated. No dental pain studies yet.

VII. Corticosteroids for Dental Pain and Inflammation Management

Agent	Approx. equiv. dose (mg)	Relative anti-inflammatory (glucocorticoid) potency	Relative mineralocorticoid (Na^+ retaining) potency	Biologic half-life (hrs)
Cortisone	25	0.8	0.8	8-12
Hydrocortisone	20	1	1	8-12
Prednisone	5	4	0.8	18-36
Prednisolone	5	4	0.8	18-36
Methylprednisolone	5	5	0.5	18-36
Dexamethasone	0.75	25	0	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 and/or Type I Diabetics
  - Severe psychiatric conditions (Schizophrenia, Bipolar Disorder, Suicidal Ideation, etc.)
  - Angle-closure glaucoma
  - Pediatric or pregnant patients

VIII. OPIOID ANALGESICS AND THEIR CHARACTERISTICS

A. OPIOIDS COMMONLY USED ORALLY FOR MILD TO MODERATE PAIN

OPIOID AVAILABLE	MME ORAL POTENCY	PEAK (HR)	DURATION (HR)	COMMENTS	PRECAUTIONS
Codeine (avoid in pts. On $2D_6$ inhibitors* - Prozac, Paxil, Cymbalta)	0.15	1.5-2	4-6	2D6 polymorphism may cause toxicity-not for pediatric patients	Impaired ventilation, asthma, high intracranial pressure,avoid in children
Hydrocodone (Norco,Lortab,G)	1.0	2	4-6	not useful after 10mg q 3 hr	Schedule II but less euphoria and more adverse effects than Oxy
Morphine (immediate release dosage form)	1.0	1.5-2	4-5	Recommended by AAP for mod-severe peds pain	Not dependent on Phase I metabolism
Hydromorphone (Dilaudid,G)	4.0	1-1.5	4-5	Potent oral morphine,high abuse potential	Not dependent on Phase I metabolism
Meperidine (Demerol,G)	0.1	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 (plain, Percocet,G)	1.5	1	3-4	not useful after 10mg q 3 hr	always a C II substance as it causes euphoria
Tramadol (avoid in pts. On 2D6 inhibitors*)	0.1	1	3-4	2D6 polymorphism may cause toxicity-not for peds	Schedule IV CS, AVOID in children

***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. Maximum 4tabs/24 hours

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. Maximum 4tabs/24 hours

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 but NOT for 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

STARTING OPIOIDS IN AN OPIOID-NAIVE PATIENT BASED ON CDC ACUTE PAIN GUIDELINES PUBLISHED NOVEMBER 2022

- **Starting dose should be 5-10 MME**
  - **That equals 5-10mg of hydrocodone**
  - **That equals 5mg of oxycodone**
- **Total dose per day should not exceed 20-30 MME**
  - **That equals 4-6 tablets of 5mg hydrocodone**
  - **That equals 3-4 tablets of 5mg oxycodone**
- **Little benefit from escalating to 50 MME per day**
  - **Most patients do NOT receive additional benefit**
  - **The harms of 50 MME and greater exceed the pain relief benefits**
- **Most dentists and OMS have stopped prescribing with the sig:**
  - **Take 1-2 tablets every 4-6 hours as needed for pain.**
- **Better sig is: Take one tablet every six hours. Maximum dose is 4 tablets per 24 hours.**

NOTE: Oxycodone/APAP available in FOUR combinations (2.5/325, 5/325, 7.5/325, 10/325)

D. 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)**
3. **ADVIL DUAL ACTION OTC**

E. 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.

PEDIATRIC ANALGESIC DOSAGES FOR DENTAL PAIN

	ONSET (min)	PEAK (hrs)	DURATION (hrs)	PEDIATRIC DOSE (mg/day)	AVAILABLE PEDIATRIC PREPARATIONS
Non-Opioids					
Acetaminophen (Tylenol, Tempra, Panadol,	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
Ibuprofen (Advil, Children's Motrin, Medipren, Nuprin, g)	20-30 30 30-45 30-45 18	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 Liquigels: Advil minis 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	11mg/kg/day (max 1650mg/day)	Tablets: 220,275, 500mg Caplets: 220mg
Opioids					
Codeine (sulfate or phosphate) **(ultra-fast metabolizers can Suffer toxic effects)-BLACK BOX WARNING in children under the age of 12years. DON'T USE.**	15-30	0.5-1	3-6	0.5mg/kg q4 hr (max120mg/day)	Codeine/APAP elixir: 12mg/120mg per 5ml susp: 12mg/120mg/5ml
Hydocodone (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.**	30-60	1-2	4-6	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)
Hydromorphone (Dilaudid,g) **(Not dependent on CYP450 for Activation/metabolism)**	20-30	1	4-5	0.03-0.1mg/kg every 4-6h	Oral Solution: 1mg/ml Tabs: 2mg,4mg,8mg
Morphine (immediate release) **Not dependent on CYP450 for Activation/metabolism**	15-20	1.5-2	4-5	0.2-0.5mg/kg Every 4-6h	Oral Solution:2,4,20mg/ml Tabs:15mg, 30mg Rectal Supp: 5,10,20,30
Oxycodone (immediate release) **(Depends on CYP450 3A4 for metabolism & 2D6 converts 10-19% to active metabolite)**	15-30	1-2	4-6	0.05-0.15mg/kg Every 4-6h	Oral Solution: 1 & 20mg/ml Tabs: 5,7.5,10,20,30mg Rectal Supp: 10 & 20mg

Drug Interactions Important in Clinical Dentistry

DENTAL DRUG	INTERACTING DRUG	RESULT/MANAGEMENT
ANTIBIOTICS		
Penicillins		
All Penicillins	Bacteriostatic antibiotics (clindamycin, erythromycin, tetracyclines)	Static agent may impair action of penicillins. Consult with other prescriber for modification.
	Methotrexate (Rheumatrex, g)	High dose penicillins may decease MTX secretion. Monitor MTX.
	Oral contraceptives	Rare decrease in estrogen effect. Use barrier contraception for duration of pill cycle.
	Probenecid (Benemid, g)	Tubular secretion of penicillins may be decreased. Usually not problematic.
Ampicillin	Allopurinol (Zyloprim, g)	Doubling in rate of ampicillin rash with concurrent administration (14-22%)
	Atenolol (Tenormin, g)	Atenolol bioavailability may be reduced.
Cephalosporins		
All Agents	Anticoagulants (Coumadin, g)	Risk of bleeding disorders might be increased in anticoagulated patients. Use cautiously.
	Bacteriostatic antibiotics (clindamycin, erythromycin, tetracyclines)	Static agent may impair action of cephalosporins. Consult with other practitioner for modification.
	Probenecid (Benemid, g)	Tubular secretion of penicillins may be decreased. Usually not problematic.
Cefdinir (Omnicef) Cefpodoxime (Vantin) Cefuroxime (Ceftin)	**Increased gastric Ph.** **(Antacids, Axid, Pepcid, Prilosec, Tagamet, Zantac)**	**Reduced absorption of the cephalosporins. AVOID CONCURRENT USE.**
Lincomycins		
Clindamycin (Cleocin, g)	Erythromycin (all macrolides)	Possibility of antagonism. AVOID CONCURRENT USE.
	Kaolin-Pectin	Delay in clindamycin absorption with concurrent use.
	Succinylcholine (Anectine)	Possibility of prolonged respiratory depression. Monitor patient.
Macrolides/Azalides	Alfentanil	Alfentanil actions increased. Use caution.
Azithromycin (Zithromax,Zpak,g) –only agent that does not inhibit CYP450 3A4 but DOES prolong QT interval so only QT prolongation interactions apply to Azithromycin	Anticoagulants (Coumadin, g)	Risk of bleeding disorders is increased in anticoagulated patients. Monitor pt.
	Benzodiazepines (alprazolam, diazepam, triazolam)	Increased benzodiazepine levels resulting in CNS depression. Avoid combination in elderly.
dirithromycin (Dynabac) clarithromycin (Biaxin, Biaxin XL, g) erythromycin (base, EC, EES, PCE)		
	Bromocriptine (Parlodel)	Increase in bromocriptine toxic effects. Consult MD.
	CCBs (diltiazem (Cardizem,g) and verapamil (Isoptin, Calan, Verelan,g)	**QT interval prolongation, sudden death, AVOID CONCURRENT USE**
	Carbamazepine (Tegretol, g)	Increased carbamazepine levels. Avoid concurrent use. Azithromycin is okay.
	Clindamycin	Possible antagonism. AVOID COMBINATION.
	Cyclosporine (Sandimmune, Neoral)	Increased cyclosporine renal toxicity. Consult MD.
	Digoxin	Increased digoxin levels in 10% of patients. May use cautiously.
	Disopyramide (Norpace, g)	Increased disopyramide levels may cause arrhythmias. Use cautiously.

Rare decrease in OC effectiveness with >48 hours of antibiotic therapy. Recommend additional barrier contraception for the remainder of the Pill package.

Macrolides(excluding azithromycin)	Ergotamine	Acute ergotamine toxicity. Use cautiously
	Methylprednisolone	Steroid clearance may be decreased. Caution.
	Penicillins	possible antagonism. Avoid static with cidal
	Pimozide (Orap)	Avoid all macrolides-risk of sudden death
	SSRIs (citalopram, escitalopram,fluoxetine, Sertraline, vilazodone)	AVOID CONCURRENT USE MACROLIDES DECREASE METABOLISM OF LISTED SSRIS.MONITOR..
	"**Statins" (except fluva-,pitava-prava)**	**Increased statin levels with possible muscle toxicity. AVOID CONCURRENT USE**
	Theophyllines	Increased theophylline levels (20-25%). Decreased erythromycin levels may also occur. AVOID CONCURRENT USE if possible. SBE prophylaxis should not cause problems.
	Tolterodine (Detrol)	Increased Detrol effects causing arrhythmias
Metronidazole (Flagyl, Flagyl ER, Prostat, g)	Anticoagulants (Coumadin)	Risk of bleeding disorders is increased in anticoagulated patients. Consult MD.
	Barbiturates	Decreased metro. Levels. Increase dose.
	Cholestyramine (Questran, g)	Reduced absorption of metronidazole
	Cimetidine (Tagamet, g)	Metronidazole levels may increase. Not sig.
	Disulfuram (Antabuse)	Concurrent use may result in acute psychosis or confusion.
	Ethanol (IV diazepam, IV TMP-SMZ)	**Risk of disulfuram-type reaction. AVOID CONCURRENT USE**.
	Lithium	Increased lithium levels with possible toxicity. Consult MD.
	Phenytoin (Dilantin)	Eff. of phenytoin may be incr. Monitor closely.
	Quinidine	Increased Quinidine levels. Monitor closely.
	Tacrolimus (Prograf)	Metronidazole doubles Prograf levels
Tetracyclines		
All Agents (doxycycline, minocycline, tetracycline)	Antacids containing Al, calcium, magnesium	Reduced serum concentrations of tets. Space administration by 1-2 hours.
	Bismuth (Pepto-Bismol)	Inhibition of tetracycline absorption. Avoid concomitant administration.
	Iron Salts	Decreased absorption of tets. Space use by 2-3h.Doxy always affected.
	Oral Contraceptives	Slightly increased risk of ovulation. Use additional method during cycle.
Doxycycline (Vibramycin, Periostat??)	Carbamazepine (Tegretol)	Metabolism of doxy increased. Monitor response to doxycycline.
	Methotrexate (highdose IV)	**AVOID DOXYCYCLINE WITH IV METHOTREXATE**
	Phenobarbital	Decreased serum levels and effect of doxy. Monitor clinical response.
	Phenytoin (Dilantin, g)	Phenytoin stimulates doxy metabolism. Increase doxy dose or use other tet.
Tetracycline (Sumycin, Panmycin)	Colestipol (Colestid)	Colestipol binds tet in intestine. Do not administer concomitantly.
	Food (Milk and Dairy)	Decreased absorption of tet. Space use by 2-3 hours.
	Zinc sulfate	Tetracycline absorption is decreased. Space use by 2-3 hours.
Quinolones: all prolong QT interval		
All Agents:	Antacids	Decreased quinolone absorption. AVOID
Ciprofloxacin (Cipro,g))	(iron, sucralfate, zinc)	CONCURRENT USE.
Levofloxacin (Levaquin)	Anticoagulants (Coumadin, g)	Increased risk of bleeding disorders. Monitor
Moxafloxacin (Avelox)		INR.
Ofloxacin (Floxin)	Antineoplastics	Quinolone serum levels may be decreased.
	Cimetidine (Tagamet, g)	Quinolone serum levels may be increased.
	Cyclosporine (Sandimmune, Neoral)	Cyclosporine renal toxicity may be enhanced.
	NSAIDs	Enhanced CNS stimulation
	Probenecid (Benemid, g)	Quinolone serum level may be increased50%.
	Theophylline	Increased theophylline toxicity possible with
Ciprofloxacin	Caffeine	Cipro and other. Consult MD Increased caffeine effects are possible.

ANTIFUNGALS	Anticoagulants (Coumadin)	Increased risk of bleeding disorders in anticoagulated patient. Consult MD.
Systemic Azole Agents (fluconazole, itraconazole, ketoconazole): all agents prolong QT interval		
	Benzodiazepines	Alprazolam, triazolam are contraindicated with itraconazole and ketoconazole. AVOID
	Cyclosporine (Sandimune, Neoral)	Increased cyclosporine levels. Can be used to the patients advantage.
	Rifampin	Decreased levels of the antifungal. AVOID CONCURRENT USE.
	"Statins" (except fluva-,pitava-prava.)	Increased levels and SE of statins.
	Tolterodine (Detrol, Detrol LA)	**Increased Detrol-causing arrhythmias.AVOID**
	Zolpidem (Ambien)	Increased Ambien effect. Caution.
fluconazole (Diflucan)	Cimetidine (Tagamet, g)	Reduced fluconazole levels. AVOID CONCURRENT USE.
	Citalopram (Celexa,g)	**QT interval prolongation.AVOID COMBO.**
	Hydrochlorothiazide	Increased fluconazole levels.
	Losartan (Cozaar, Hyzaar)	Increased Losartan hypotension effect
	Oral Contraceptives	Increased estrogen levels BUT UNLIKELY TO INTERFERE WITH OC EFFECTIVENESS
	Phenytoin (Dilantin, g)	Increased phenytoin levels. Monitor carefully.
	Sulfonylureas	Increased hypoglycemic effect. Monitor blood glucose.
itraconazole (Sporonax)	Digoxin	Increased digoxin levels. AVOID COMBINATION.
	Increased gastric pH	Reduced itraconazole levels
	Isoniazid (INH)	Reduced itraconazole levels
	Losartan (Cozaar)	Increased Losartan hypotension effect
	Sulfonylureas	Increased hypoglycemic effects. Monitor blood glucose.
ketoconazole (Nizoral, g)	Corticosteroids	Possible increase in steroid levels.
	Increased gastric pH	Decreased ketoconazole levels. AVOID CONCURRENT USE.
	Isoniazid (INH)	Decreased ketoconazole levels
	Theophyllines	Decreased theophylline levels. Consult with MD.
NON-NARCOTIC ANALGESICS		
NSAIDS		
(including aspirin and COX-2s)	**Anticoagulants (apixaban, dabigatran,edoxaban,,rivaroxaban,warfarin)**	**Increase risk of bleeding disorders in anticoagulated patient. AVOID COMBO**
	Antihypertensives (all but CCBs)	Decreased antihypertensive effect. Monitor Blood Pressure.
	(ACEI,B-blockers, diuretics)	
	Cimetidine (Tagamet, g)	NSAID levels increased/decreased
	Cyclosporine (Neoral, Sandimmune)	Nephrotoxicity of both agents may be increased. Avoid if possible.
	Combo of ACEor ARB & Diuretic	**30% increase in risk of kidney injury-called the TRIPLE WHAMMY on the kidney!**
	Fluoroquinolones	Increased CNS stimulation
	Lithium	Increased lithium levels. Use sulindac
	Methotrexate (Rheumatrex, Mexate)	Toxicity of methotrexate may be increased. Monitor.
	Phenytoin (Dilantin, g)	Increased phenytoin levels
	Probenecid (Benemid, g)	Increased toxicity of NSAIDs possible.
	Salicylates	**Decreased NSAID levels with increased GI effects. AVOID CONCURRENT USE.**
	SSRIs	Possible increased risk of bleeding but not thought to be clinically significant
COX-2 SELECTIVE NSAID		
Celecoxib (Celebrex)	$2C_9$ inhibitors (fluconazole)	Increased celecoxib levels

Ibuprofen (Motrin, g)	Digoxin	Possible increase in digoxin levels.
Ketorolac (Toradol,g)	Salicylates	Increased Ketorolac free drug conc.
Sulindac	DMSO	Decreased sulindac effectiveness and severe peripheral neuropathy. Avoid concurrent use.
Sulindac	Lithium	Lithium levels remain constant or decrease.
Acetaminophen only	Barbiturates, Carbamazepine, Phenytoin, Rifampin, Sulfinpyrazone	The hepatotoxicity of APAP may be increased by high dose or long term administration of these drugs.
	Cholestyramine (Questran, g)	Decreased APAP absorption. Do not administer within 2 hours of each other.
	Ethanol	Increased hepatotoxicity of APAP with chronic ethanol ingestion.
Tramadol (Ultram, Ultracet, g)	**Any drug that enhances serotonin activity(SSRI antidepressants,"triptans" for acute migraine**	**Possible serotonin syndrome. AVOID CONCURRENT USE**.
	Carbamazepine (Tegretol,g)	Decreased tramadol levels
	MAOI's ()	MAOI toxicity enhanced
	Quinidine	Tramadol increased/metabolite decreased
	Ritonavir (Norvir)	Increased Tramadol effect. AVOID COMBO.
NARCOTIC ANALGESICS		
Opioid analgesics	Alcohol, CNS depressants, local anesthetics, antidepressants, antipsychotics, antihistamines, cimetidine	Increased CNS and respiratory depression may occur. Use cautiously.
	Antimuscarinics and antidiarrheals (e.g. atropine), antihypertensives (e.g. guanadrel)	Opioids increase the effects of these drugs. Use cautiously.
	Buprenorphine, nalbuphine, naltrexone	These drugs block the analgesic effects of opioids. Substitute with NSAIDs.
	Lybalvi (olanzepine/samidorphan)	**Samidorphan is an opioid antagonist so d/c 7 days prior to use of opioid analgesic**
Codeine (Hydrocodone lesser extent)	$2D_6$ Inhibitors, Amiodarone, Cimetidine, Desipramine, Fluoxetine, Paroxetine, Propafenone, Quinidine, Ritonavir	Inhibition of biotransformation of Codeine to active analgesic form. Use different narcotic on $2D_6$ Inhibitor patients.
Meperidine (Demerol, g)/Fentanyl/All Fentanyl derivatives	**MAOIs (Marplan, Nardil, Parnate, Furoxone) selegiline (Eldepryl)**	**Hypertension/hyperpyrexia or coma and hypotension.AVOID CONCURRENT USE if MAOI taken within 14 days**.
	Protease inhibitors	Increased CNS/resp. depression- AVOID
	Ritonavir (Norvir)	Large increase in meperidine. AVOID COMBO.
LOCAL ANESTHETICS	Alcohol,CNS depressants,opioids, antide-pressants,antipsychotics, antihistamines	Increased CNS and resp. depression may occur. Use caution.
	Antiarrhythmic drugs	Increased cardiac depression.
Amides (e.g. lidocaine)	Beta Blockers, cimetidine	Metabolism of lidocaine is reduced. Use caution
Esters (e.g. procaine)	Anticholinesterases (Neostigmine) Sulfonamides	Metabolism of esters reduced. Inhibit sulfonamide action.
VASOCONSTRICTORS (epinephrine,levo-nordefrin)	Inhalation anesthetics (halothane)	Increased chance of arrhythmia
	Tricyclic antidepressants-high dose (amitriptyline, desipramine, imipramine, nortriptyline, etc)	Increased sympathomimetic effects possible. Limit epi to 0.04mg with high dose TCA's.
	Beta-blockers (nonselective)	Hypertensive and/or cardiac rx possible.
	(e.g. propranolol, nadolol)	Limit epi to 0.04mg/2hr. visit.
	Phenothiazines (e.g. chlorpromazine)	Vasoconstrictor action inhibited,leading to possible hypotensive responses. Use cautiously.
	Monoamine Oxidase Inhibitors (MAOIs)	Slight possibility of hypertensive rx.
	Selegiline (Eldepryl,g)	Slight possibility of hypertensive rx.
	COMT Inhibitors (Comtan, Tasmar)	Slight possibility of hypertensive rx.

AGENTS FOR PARENTERAL ANESTHESIA		
Antihistamines		
diphenhydramine (Benadryl) hydroxyzine (Atarax, Vistaril) Promethazine (Phenergan)	Anticholinergics	Increased dry mouth, tachycardia, urinary retention. Monitor.
	CNS depressants (alcohol, narcotics)	Enhanced duration and intensity of sedation. Reduce dosages.
Barbiturates		
methohexital (Brevital,g)	CNS depressants (alcohol, narcotics)	Additive CNS and resp. depression
	Furosemide (Lasix, g)	Orthostatic hypotension
	Sulfisoxazole IV	Sulfa competes with barb. for binding sites. Smaller and more frequent barb. doses may have to be given.
Benzodiazepines		
diazepam (Valium,G)	CNS depressants (anticonvulsants, alcohol)	Oversedation so may use slower titration.
	Cimetidine,OCs,INH,Ketoconazole, Metoprolol, Omeprazole, Propoxyphene, Propranolol,Valproic Acid	Decreased clearance of diazepam. Can avoid with lorazepam.
	Digoxin	Increased digoxin levels.
midazolam (Versed,g)	Calcium Channel Blockers or CCBs (diltiazem-Cardizem, verapamil-Isoptin,Calan, Verelan)	CCBs inhibit Cyp3A4 which prolongs the actions of midazolam. Evaluate patient factors to determine clinical significance.
	CNS depressants (alcohol, barbs)	Increased risk of underventilation or apnea. May prolong the effect of midazolam.
	Erythromycin	Increased midazolam levels. Monitor.
	Narcotics (morphine, meperidine, fentanyl)	Increased hypnotic effect of midazolam. More hypotension with Versed and Demerol.
	Saquinavir (Fortovase)	Increased midazolam levels. AVOID COMBO.
	Thiopental	After premed with Versed, decrease dose of thiopental for induction by 15%
Narcotics		
fentanyl (Sublimaze,g)	Barbiturate anesthetics	Additive CNS and resp. depression.
	Chlorpromazine (Thorazine, g)	Increased toxicity of both agents.
	Cimetidine (Tagamet, g)	CNS toxicity case reports only. (confusion, apnea,
	Citalopram (Celexa,g)	Increased risk of serotonin syndrome
	Diazepam	With high dose fentanyl gives CV depression.
	Droperidol (Inapsine)	Hypotension < pulmonary arterial pressure.
	MAOIs and furazolidone (Furoxone)	**Risk of hypertensive crisis.AVOID COMBO**
	Nitrous Oxide	With high dose fentanyl may cause CV depress.
	Ritonavir (Norvir)	Increased fentanyl levels with Norvir
meperidine (Demerol, G)	Barbiturate anesthetics	Additive CNS and resp. depression
	Chlorpromazine (Thorazine, g)	Increased toxicity of both agents.
	Cimetidine (Tagamet, g)	CNS toxicity as with fentanyl.
	MAOIs and furazolidone (Furoxone)	**Meperidine has predictable and sometimes fatal reactions with use within 14 days. Typel :coma,resp dep,cyanosis,low BP Type2:seizures,hyperpyrexia,hypertension,tachy-cardia. AVOID CONCURRENT USE!!!!!**
	Phenytoin (Dilantin, g)	Decrease meperidine effects by increased hepatic metabolism
Miscellaneous		
etomidate (Amidate)	Verapamil	Possibility of prolonged anesthesia
ketamine (Ketalar,g)	Barbiturates	Prolonged recovery time.
	Thyroid Hormone	May produce hypertension/tachycardia
	Tubocurarine and nondepolarizing muscle relaxants	Ketamine may increase neuromuscular effects and result in prolonged resp. depression.
Propofol (Diprivan, G)	CNS depressants (sedative/hypnotic, inhalation anesthetics, narcotics)	Increase CNS depression of propofol. Premed with narcotics may lead to more pronounced decrease in systolic, diastolic, and mean arterial pressures and cardiac output.