

NEW STRATEGIES FOR TARGETING ANTIBIOTIC USE IN CLINICAL DENTISTRY

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I. TARGETED INDICATIONS IN DENTAL PRACTICE

A. Therapeutic Indications

1. Acute cellulitis of dental origin
2. Acute pericoronitis with elevated temperature and trismus
3. Deep fascial space infections
4. Open fractures of the mandible and maxilla
5. Extensive, deep, or old (>6hours) orofacial lacerations
6. Dental infection or oral surgery in the compromised host

B. Prophylactic Indications

1. Prosthetic heart valve or valve repair
2. Hx of endocarditis or severe congenital abnormality
3. Total Joint Arthroplasty – www.Orthoguidelines.org/AUC

C. Antibiotics NOT Generally Indicated in Endodontics

Pain Without Signs and Symptoms of Infection
• Symptomatic irreversible pulpitis
• Symptomatic apical periodontitis (Pain to percussion and biting)
Teeth with Necrotic Pulps and a Radiolucency
Teeth with a Sinus Tract/Parulis (Chronic Apical Abscess)
Acute Apical Abscess in Immunocompetent Patients <i>(When same visit treatment is an option)</i>
• Localized fluctuant swellings

D. Adjunctive Antibiotics Indicated in Endodontics

Acute Apical Abscess in Immunocompromised Patients
• Localized fluctuant swellings
• Patient with systemic disease causing impaired immunologic function
Acute Apical Abscess in Immunocompetent Patients <i>(When same visit treatment is not an option)</i>
• Localized fluctuant swellings
Acute Apical Abscess with Systemic Involvement
• Elevated body temperature >100°F
• Malaise
• Unexplained trismus
• Lymphadenopathy
Progressive Infections
• Rapid onset of swelling <24hrs
• Cellulitis or a spreading infection
• Osteomyelitis
Persistent Infection
• Chronic exudation, which is not resolved by regular intracanal procedures and medications

E. When to Refer to a Specialist and/or Hospital-Based Care

- Rapidly progressive infection
- Difficulty in breathing and/or swallowing
- Fascial space involvement
- Elevated temperature (greater than 101°F)
- Severe Trismus (less than 10 mm)

II. TARGETED PATIENTS AT INCREASED RISK OF OROFACIAL INFECTIONS DUE TO DRUG THERAPY OR DISEASE STATE

A. Patient-Specific Risk Factors

1. **Immunocompromised** by drug therapy or disease process
 - a. drug therapy – TNFIs, Biologics, systemic prednisone > 10mg/day organ transplant rejection drugs, etc.
 - b. disease process – SLE, rheumatoid arthritis, malnutrition, neoplastic disease, poor glycemic control in diabetics (A1c > 8%)
2. **Impaired by trauma, surgery, reduced circulation, or implanted device**
 - a. hematomas and scar tissue – promote bacterial proliferation
 - b. reduced circulation – may prevent antibiotic from reaching site
 - c. implanted devices – intravascular devices are the leading cause of nosocomial infections and increase risk of endocarditis in some cases
3. **Renal Insufficiency**
 - a. Tetracycline HCl contraindicated but doxycycline and minocycline are NOT Contraindicated and dose reductions are not necessary
 - b. Dosage reduction for most beta-lactams, clarithromycin & most quinolones
 - c. No dosage reduction necessary for azithromycin, cefuroxime, clindamycin, dicloxacillin, doxycycline, erythromycin, metronidazole, minocycline, moxifloxacin, nafcillin
 - d. **Renal failure is defined by the following stages:**



4. **Hepatic Impairment:** dosage adjustment needed: clindamycin & metronidazole
5. **Diabetic Glycemic Control**

Correlation Between A1c and Mean Plasma Glucose

A1c (%)	Mean plasma glucose
6	126mg/dl
7	154mg/dl
8	183mg/dl
9	212mg/dl
10	240mg/dl
11	269mg/dl
12	298mg/dl

← Patient Risks Increased

Importance of Glycemic Control in Dental Patients

- Prevention of hyperglycemia AND hypoglycemia
- Nonketotic hypertonicity/ketoacidosis
- Impaired wound healing & Increased risk of oral infections
- Delayed gastric emptying could lead to aspiration during a procedure

ADA Clinical Practice Guideline on the Use of Antibiotics for the Emergency Management of Symptomatic Irreversible Pulpitis, Symptomatic Apical Periodontitis, and Localized Acute Apical Abscess. Found at www.ada.org/ebd/files/Antibiotics_Recommendations

Setting	Clinical questions	Expert panel recommendations and good practice statements
Emergent situations where dental care is available, but pulpotomy, pulpectomy, root canal debridement, non-surgical root canal treatment, or incision for drainage of abscess are not an immediate option (same visit).	1. For immunocompetent adults with symptomatic irreversible pulpitis¹ with or without symptomatic apical periodontitis,² should we recommend the use of oral systemic antibiotics compared to the non-use of oral systemic antibiotics to improve health outcomes?	Recommendation: The expert panel does not recommend dentists prescribe oral systemic antibiotics for immunocompetent adults with symptomatic irreversible pulpitis ¹ with or without symptomatic apical periodontitis, ² due to the lack of improvement in health outcomes and substantial individual and community level harms associated with prescribing antibiotics. ³ Clinicians should refer ⁴ patients for definitive treatment in a timely manner while providing interim monitoring. ⁵ (Strength of Recommendation: Strong, Certainty in the Evidence: Low).
	2. For immunocompetent adults with pulp necrosis and symptomatic apical periodontitis² or localized acute apical abscess,⁶ should we recommend the use of oral systemic antibiotics compared to the non-use of oral systemic antibiotics to improve health outcomes?	A. Recommendation: The expert panel does not suggest dentists prescribe oral systemic antibiotics for immunocompetent adults with pulp necrosis and symptomatic apical periodontitis, ² due to the lack of improvement in health outcomes and substantial individual and community level harms associated with prescribing antibiotics. ³ Clinicians should refer ⁴ patients for definitive treatment in a timely manner while providing interim monitoring. ⁵ If definitive treatment is not feasible, a contingency prescription [oral amoxicillin (500 milligrams, three times a day, with or without loading dose of 1,000 mg, 3-7 d) or penicillin VK (500-600 mg, four times a day, 5-7 d)] ^{7,8} (delayed prescribing, watchful waiting) should be provided (Strength of Recommendation: Conditional, Certainty in the Evidence: Very low). B. Recommendation: The expert panel suggests dentists prescribe oral amoxicillin (500 milligrams, three times a day, with or without loading dose of 1,000 mg, 3-7 d) or penicillin VK (500-600 mg, four times a day, 5-7 d) ⁸ for immunocompetent adults with pulp necrosis and localized acute apical abscess. ⁶ Clinicians should additionally provide urgent referral ⁴ as definitive treatment should not be delayed ⁵ (Strength of Recommendation: Conditional, Certainty in the Evidence: Very low).
	3. For immunocompetent adults with pulp necrosis and acute apical abscess with systemic involvement,⁹ should we recommend the use of oral systemic antibiotics compared to the non-use of oral systemic antibiotics to improve health outcomes?	Good practice statement: The expert panel suggests dentists prescribe oral amoxicillin (500 milligrams, three times a day, with or without loading dose of 1,000 mg, 3-7 d) or penicillin VK (500-600 mg, four times a day, 5-7 d) ⁸ for immunocompetent adults with pulp necrosis and acute apical abscess with systemic involvement. ⁹ Clinicians should additionally provide urgent referral ⁴ as definitive treatment should not be delayed. ⁵ If the clinical condition worsens or if there is

Setting	Clinical questions	Expert panel recommendations and good practice statements
		concern for deeper space infection or immediate threat to life, refer patient for emergent medical evaluation.
Emergent situations where dental care is available, and pulpotomy, pulpectomy, or root canal debridement, non-surgical root canal treatment, or incision for drainage of abscess are an immediate option (same visit).	4. For immunocompetent adults with symptomatic irreversible pulpitis¹ with or without symptomatic apical periodontitis,² should we recommend the use of oral systemic antibiotics compared to the non-use of oral systemic antibiotics as an adjunct to dental treatment ¹⁰ to improve health outcomes?	Recommendation: The expert panel does not suggest dentists prescribe oral systemic antibiotics as an adjunct to dental treatment ¹⁰ for immunocompetent adults with symptomatic irreversible pulpitis ¹ with or without symptomatic apical periodontitis, ² due to the lack of improvement in health outcomes and substantial individual and community level harms associated with prescribing antibiotics ³ (Strength of Recommendation: Conditional, Certainty in the Evidence: Low).
	5. For immunocompetent adults with pulp necrosis and symptomatic apical periodontitis² or localized acute apical abscess,⁶ should we recommend the use of oral systemic antibiotics compared to the non-use of oral systemic antibiotics as an adjunct to dental treatment ¹¹ to improve health outcomes?	Recommendation: The expert panel does not recommend dentists prescribe oral systemic antibiotics as an adjunct to dental treatment ¹¹ for immunocompetent adults with pulp necrosis and symptomatic apical periodontitis ² or localized acute apical abscess, ⁶ due to the lack of improvement in health outcomes and substantial individual and community level harms associated with prescribing antibiotics ³ (Strength of Recommendation: Strong, Certainty in the Evidence: Low).
	6. For immunocompetent adults with pulp necrosis and acute apical abscess with systemic involvement,⁹ should we recommend the use of oral systemic antibiotics compared to the non-use of oral systemic antibiotics as an adjunct to dental treatment ¹¹ to improve health outcomes?	Good practice statement: The expert panel suggests dentist perform urgent dental treatment ¹¹ in conjunction with prescribing oral amoxicillin (500 milligrams, three times a day, with or without loading dose of 1,000 mg, 3-7 d) or penicillin VK (500 milligrams, four times a day, 5-7 d) ⁸ for immunocompetent adults with pulp necrosis and acute apical abscess with systemic involvement. ⁹ If the clinical condition worsens or if there is concern for deeper space infection or immediate threat to life, refer for emergent medical evaluation.

6. Reasons Why Antibiotics Fail

- Inadequate drainage or debridement
- Antibiotic does not reach infection site
- Physical obstruction or open access
- Systemic disease alters host response
- Foreign body reaction
- Patient noncompliance
- Inadequate dose or duration
- Wrong antibiotic is chosen
- Development of bacterial resistance
- Concomitant therapy interferes

Pitfalls in Antibiotic Prescribing

Antibiotic adverse effects not considered
 Cost of antibiotic not considered
 Rapid and inappropriate therapy changes
 Patient is not counseled or monitored
 Inappropriate drug or dosage regimen
 Failure to correct contributing factors
 Continuing antibiotics too long after

7. Recommended Antibiotics in Endodontics and Dosages

DRUG OF CHOICE	LOADING DOSE <small>****Conditional recommendation</small>	ADULT MAINTENANCE DOSE
Amoxicillin w/ clavulanic acid	1000 mg 1000 mg	500 mg q8 h 3-7 days 500/125 mg q8h 7 days
Penicillin VK	1000 mg	500 mg q4-6 h 3-7 days
Azithromycin <small>*Penicillin allergy w/ hx of hives, angioedema, or anaphylaxis</small>	500 mg	250 mg q24h (5 days including loading dose)
Cephalosporins (Cephalexin) <small>*Penicillin allergy w/o hx of hives, angioedema, or anaphylaxis</small>	1000 mg	500 mg q6h 3-7 days
Clindamycin <small>*Penicillin allergy w/ hx of hives, angioedema, or anaphylaxis</small>	600 mg	300 mg q6 h 3-7 days
Metronidazole <small>**Complement antibiotic</small>	1000 mg	500 mg q8h 5-7 days
Erythromycin <small>***Historical Antibiotic</small>	500 mg	250 mg q4-6h 7-10 days
Ciprofloxacin	500 mg	250-500 mg q6h x 7-10 days

*Comparative safety and effectiveness of common antibiotics with Penicillin **Provides great gram-negative anaerobic activity
 essentially not effective against anaerobic *Facility specific recommendations

III. TARGETED ANTIBIOTIC SELECTION

A. Mechanism of action and spectrum of activity

BACTERIOSTATIC

Tetracyclines

Sulfonamides

Linezolid

Macrolides

Azalides

Clindamycin(static/Cidal)

BACTERICIDAL

Penicillins

Cephalosporins

Carbapenems

Vancomycin

Metronidazole

Fluoroquinolones

All Beta-lactams

SPECTRUM OF ACTIVITY

Narrow

Metronidazole

Penicillin VK

Dicloxacillin

Nafcillin

Cefazolin

Clindamycin

Cephalexin

Extended

Amoxicillin

Azithromycin

Cefuroxime-axetil

Cefaclor

TMP-SMZ

Broad/Very Broad

Tetracyclines

Carbapenems

Doxycycline

Minocycline

Amox/Clav

(Augmentin)

Levofloxacin

Moxifloxacin

B. Activity Against Common Oral Pathogens

Aerobic Bacteria

Gram-positive cocci

Streptococcus

Viridans (facultative)

B-Hemolytic

Staphylococcus

Gram-positive bacilli

Actinomyces (facultative)

Lactobacillus (facultative)

Frequency

very common

unusual

rare

less common

less common

Anaerobic Bacteria

Gram-positive cocci

Peptostreptococcus

Gram-negative bacilli

Porphyromonas (Bacteroides)

Prevotella spp (Bacteroides)

Fusobacterium spp

Bacteroides fragilis

Frequency

common

less common

very common

common

rare

1. The typical odontogenic infection is composed of a mix of aerobic and anaerobic species

2. The timeline of infection may show: AEROBES-----MIXED-----ANAEROBES.

3. Obtain cultures & sensitivities for: antibiotic failures, recalcitrant infections, suspected osteomyelitis, impaired host defenses, post-op wound infections, etc.. REMEMBER-anaerobes outnumber aerobes by a ratio of 3:1.

IV. ANTIBIOTIC THERAPY GUIDELINES

A. Antimicrobial prescribing in the USA is 80 % empirical therapy.

1. Target causative organism -empirical or lab
2. Patient drug and medical history - ALLERGIES vs ADVERSE REACTIONS?? Use Johns Hopkins Flow Chart
3. Patient counseling - adverse effects, compliance, therapeutic endpoints, cost
4. Positive response expected in 48 hours, continue therapy 24 hours after symptom resolution
5. Combination therapy: 3 possible effects - indifferent (additive) - synergism – antagonism
Cidal + Cidal *or* Static + Static
6. Best combination: penVK qid + metronidazole qid, or amoxicillin tid + metronidazole tid

V. ANTIBIOTIC CLASSES

A. ORAL PENICILLINS – FDA Pregnancy Category B

ORAL PENICILLINS USEFUL IN DENTISTRY						
Classification	t ¹ / ₂ (h)	OK with food?	Pediatric Dose	Activity against oral pathogens		
				Gm ⁺ Aerobes	Gm ⁺ Anaerobes	Gm ⁻ Anaerobes
<u>Natural</u> Penicillin G Penicillin VK	1 1	no yes	150-250K U/kg/d 25-50mg/kg/day	+ +	+ +	+ +,-
<u>Penicillinase-Resistant</u> Dicloxacillin Nafcillin	.75 .75	no no	12-25mg/kg/day 37mg/kg q 6h	staph only staph+strep	- -	- -
<u>Aminopenicillins</u> Amoxicillin Amox/potassium clavulanate (Augmentin, G) Ampicillin	1.5 1.5 1.5	yes yes no	40-50mg/kg/day 40-45mg/kg/day 50-100mg/kg/day	+ + +	+ + -	- + +,-

1. INDIVIDUAL AGENTS

Amoxicillin advantages over penicillin

- more complete absorption
- longer duration of activity
- TID administration

Amoxicillin disadvantages over Pen VK

- broader spectrum
- poor anaerobe activity
- more side effects/less efficacy

2. ADVERSE EFFECTS

Hypersensitivity

- 3 - 10 % of population is allergic to penicillins (more frequently with IV/IM than PO route)
- IgE Mediated acute reaction - PCN binds to protein and acts as a hapten to which Ab develop
- True anaphylactic reactions to penicillin are 1/7,000 to 1/25,000 instances of PCN use
 - *mortality occurs once in every 50,000 - 60,000 treatment courses
 - * sx. begin 10-20 min. after ingestion, antihistamines are of little effect
- Cross-reactivity to cephalosporins occurs in 3-5% of patients (lowest risk is ceftriaxone)
 - *Cephalosporins are contraindicated with pt history of severe or immediate penicillin reaction (urticaria, angioedema, anaphylaxis)

3. JOHNS HOPKINS PENICILLIN ALLERGY SCREENING TOOL WITH PICTURES

https://www.hopkinsmedicine.org/antimicrobial-stewardship/_doc/_nursing_toolkit/penicillin-allergy-algorithm-with-pictures.pdf

Useful Corresponding Article: JAMA. 2019;321(2):188-199. doi:10.1001/jama.2018.19283

4. DRUG INTERACTIONS

Bacteriostatic antibiotics
Oral contraceptives
Methotrexate

B. ORAL CEPHALOSPORINS – FDA Pregnancy Category B

Oral Cephalosporins Useful in Dentistry						
Classification	t ^{1/2} (min)	OK with food?	Pediatric Dose	activity against oral pathogens		
				Gm ⁺ Aerobes	Gm ⁺ Anaerobes	Gm ⁻ Anaerobes
<u>First Generation</u> Cephalexin (Keflex,g) Cefadroxil (Duricef,Ultracef,g)	50-80 78-96	yes yes ⁺	25-50mg/kg/d (4) 30mg/kg/day (1)	+	+	-
<u>Second Generation</u> Cefaclor (Ceclor,G) Cefuroxime-Axe (Ceftin,G) Cefprozil (Cefzil,G)	35-54 80 78	yes yes ⁺ yes ⁺	20-40mg/kg/day (3) 10-15mg/kg bid (2) 15-30mg/kg/day (2)	+	+	-
<u>Third Generation</u> Cefdinir (Omnicef) Cefixime (Suprax) Cefpodoxime (Vantin) Ceftibuten (Cedax) Cefditoren (Spectracef)	100 180-240 120-180 144 96	yes yes yes ⁺ no yes	14mg/kg/day (1-2) 8mg/kg/day (1-2) 10mg/kg/day (2) 4.5mg/kg bid None given	+	-	-

1. INDIVIDUAL AGENTS

- 1st generation: best gram + coverage of all cephalosporins
 2nd generation: best anaerobe coverage of all cephalosporins
 3rd generation: oral agents provide variable degrees of oral anaerobe activity

2. ADVERSE EFFECTS

Hypersensitivity and oral candidiasis

3. DRUG INTERACTIONS

Bacteriostatic antibiotics
 Anticoagulants
 Antacids, H₂ blockers, PPIs (cefdinir, cefuroxime)

C. ORAL MACROLIDES – FDA Pregnancy Category B (except clarithromycin = C)

Oral Macrolides Useful in Dentistry						
Drug	T _{peak} (h)	OK with food?	Pediatric Dose	activity against oral pathogens		
				Gm ⁺ Aerobes	Gm ⁺ Anaerobes	Gm ⁻ Anaerobes
<u>Erythromycin Base</u> Abbott Filmtab Boots E-Mycin (EC) Abbott Ery-Tab (EC) Abbott PCE (PC) P-D ERYC (EC)	3 6 3f, 2nf 3 3	no yes yes no? no	30-40mg/kg/day (3-4) (3-4) (3-4)	+,- +,- +,- +,- +,-	+	-
<u>Erythromycin Ethylsuccinate</u> Abbott E.E.S., generic	2	yes	Base dose x 1.6	+,-	-	-
<u>Erythromycin Stearate</u> Abbott Erythrocin	3	no	30-40mg/kg/day	+,-	-	-
Azithromycin (Zithromax,g)	2-3	Caps-no Tabs=yes	Day 1: 10mg/kg Days 2-5: 5mg/kg	+,-	+	+,-
Clarithromycin (Biaxin,g) Preg C	1.7	yes	15mg/kg/day (1-2)	+,-	+,-	+,-
Telithromycin (Ketek)	1	yes	Not approved	+	-	-

1. INDIVIDUAL AGENTS

Clarithromycin (Biaxin) advantages over erythromycin base:

- 3% GI irritation as opposed to 30% for older agents, BID dosing
- better activity against *S. pyogenes* than erythromycin, cefaclor or doxycycline
- better anaerobe coverage than erythromycin

Azithromycin (Zithromax): 2-4 fold less active than erythromycin against most strains of strep. HAS risk of QT interval prolongation. Azalide has limited drug interactions compared to macrolides

2 ADVERSE EFFECTS

Cholestatic jaundice (estolate salt = Ilosone) Taste disturbances (Clarithromycin)
 Gastrointestinal disturbances Oral candidiasis

3. DRUG INTERACTIONS

Alfentanil	Carbamazepine	Ergotamine
Anticoagulants	CCBs (diltiazem, verapamil)	“Statins”
Azole antifungals	Cyclosporine	Theophylline
Bromocriptine	Disopyramide	Tolterodine

D. ORAL FLUOROQUINOLONES – FDA Pregnancy Category C

Oral Fluoroquinolones Available in the USA						
Drug*	t ^{1/2} (h)	OK with food?	Usual Adult Dose	activity against oral pathogens		
				Gm ⁺ Aerobes	Gm ⁺ Anaerobes	Gm ⁻ Anaerobes
Ciprofloxacin (Cipro, G)	5	yes	500mg bid	-	-	-
Delafloxacin (Baxdela)	5	yes	450mg bid	+	+	+,-
Gemifloxacin (Factive,G)	7	yes	320mg qd	+	-	-
Levofloxacin (Levaquin,G)	8	yes	500mg q24 h	++	+	+,-
Moxifloxacin (Avelox,G)	10	yes	400mg qd	+	+	+,-
Ofloxacin (Floxin)	8	yes	400mg q12h	+,-	-	-

*not indicated for children or adolescents except for cystic fibrosis

1. BLACK BOX WARNING: TENDONITIS & ACHILLES TENDON RUPTURE, WORSENING MYASTHENIA GRAVIS, IRREVERSIBLE PERIPHERAL NEUROPATHY, CNS EFFECTS. AVOID IN UNCOMPLICATED INFECTIONS.

2. ADVERSE EFFECTS

Arthropathies: contraindicated for children, adolescents, pregnant or lactating women
 CNS stimulation/toxicity
 Gastrointestinal disturbances
 QT interval prolongation risk

3. DRUG INTERACTIONS

Antacids (Fe, sucralfate, zinc)	Cyclosporine
Antiarrhythmics (Spar)	NSAIDS (increased CNS stimulation)
Anticoagulants	Probenecid
Antineoplastics	Theophylline
Cimetidine	Caffeine (Cipro)

E. MISCELLANEOUS AGENTS

Miscellaneous Oral Agents						
Drug	t ^{1/2} (h)	OK with food?	Pediatric Dose	activity against oral pathogens		
				Gm ⁺ Aerobes	Gm ⁺ Anaerobes	Gm ⁻ Anaerobes
Clindamycin (Cleocin,g) FDA B	2	yes	15-30mg/kg/day (3-4)	+	+	+
Metronidazole (Flagyl,g) FDA B	8	yes	30mg/kg/day (3-4)	-	+	+
<u>Tetracyclines</u> FDA D						
Tetracycline HCL (Sumycin,g)	6-12	no	25-50mg/kg/d (4)	-	+	+,-
Doxycycline (Vibramycin,g)	15-25	yes	2-4mg/kg/day (2)	-	+	+,-
Minocycline (Minocin,g)	11-18	yes	4mg/kg x 1 day, 2mg/kg/day	-	+	+,-

1. CLINDAMYCIN is Pregnancy Category B

a). Cross-reaction with erythromycins because they are all “mycins”?? – doesn’t happen

b). Adverse effects:

Gastrointestinal disturbances & morbilliform skin eruptions

c)BLACK BOX WARNING: Clostridia Difficile Induced Colitis (CDIC)

d). Drug interactions

Succinylcholine

Erythromycin

Kaolin-Pectin

Take Home Points

- The **biggest risk factor** for CDI is antibiotics and the most common offenders include clindamycin, fluoroquinolones, cephalosporins (3rd/4th gen), and penicillins.
- **Nosocomial CDI** occurs within 1 year of hospitalization.
→ A medication that is a **risk factor for both nosocomial and community** acquired CDI is PPI.
- **50%** of Pts have positive stool PCR for as long as 6 weeks after **abx completion**.
- **2 main lab tests** that differentiate non-severe from severe infection are WBC >15 and Cr >1.5x baseline.
- New **2018 first line Tx** for an initial, non-severe infection is Vancomycin PO or Fidaxomicin PO x10 days.
→ Metronidazole PO can still be used if these are not available.
- For **fulminant colitis**, Vancomycin PO AND Metronidazole IV are given x14 days.
→ One can also consider Vancomycin enemas vs surgery in appropriate clinical situations.
- **Recurrent infection** is thought to result from persistent spores from the initial infection.
→ **1st recurrence** can be treated with fidaxomicin or a prolonged PO vancomycin pulse taper.

2. METRONIDAZOLE

- BLACK BOX WARNING:** Metronidazole has been shown to be carcinogenic when given chronically to rats and mice. Avoid use in children except for approved indication (amebiasis).
- Adverse effects – taste disturbances, peripheral neuropathy, GI irritation
 - mutagenic effect demonstrated with in vitro assays as well, turns urine reddish
- Interaction with ethanol and disulfuram (Antabuse) may lead to gastrointestinal distress and N/V. Avoid alcohol during and for 1 day after discontinuing metronidazole. Preg Category B
- Drug interactions

Anticoagulants	Disulfuram	Ethanol (IV diazepam, IV SMZ/TMP)
Lithium	Phenytoin	

3. TETRACYCLINES

- Adverse effects
 - Esophageal ulceration
 - Toxicity -outdated tetracycline is potentially renal toxic
 - Pregnancy – hepatotoxicity. Pregnancy Category D due to pediatric tooth discoloration
- Drug interactions

<u>ALL TETRACYCLINES</u>	<u>DOXYCYCLINE</u>	<u>TETRACYCLINE</u>
Antacids, bismuth	Phenobarbital	Food (milk, dairy)
Iron salts	Phenytoin	Cholestipol
Oral contraceptives		Zinc sulfate
- Periodontal infections
 - Advantages in periodontal infections:
 - high concentration in GCF
 - good activity against A.A
 - binds to root surfaces
 - anticollagenase activity
- Periodontal abscesses – tetracyclines are NOT the drugs of choice
- Compliance considerations: cost, GI irritation, doses per day

4. **OXALODINONES – Linezolid (Zyvox) 400mg and 600mg tablets**
- a) reserved for resistant gram positive pneumonias and CA-MRSA
 - b) IS effective for gram positive oropharyngeal anaerobes

F. PATIENT-SPECIFIC ANTIBIOTIC SELECTION CRITERIA

1. History of allergy to penicillin
 - a. Avoid all penicillins and don't prescribe clarithromycin due to cardiotoxicity concerns.
 - b. Avoid cephalosporins if hives, angioedema, anaphylaxis, or unknown history is reported
2. History of antibiotic-associated diarrhea
 - a. Use narrow spectrum agent if possible-consider flora support with Florajen3 probiotic supplement
Best choice is pen VK with /without metronidazole
 - b. Avoid 2nd and 3rd generation cephalosporins
 - c. Avoid clindamycin, fluoroquinolones, and amoxicillin/clavulanic acid (Augmentin,G)
3. Inadequate response to penicillin VK
 - a. Add metronidazole 1000-2000mg/day in four divided doses to pen VK
 - b. Stop pen VK and initiate clindamycin 300mg qid or q 6h.
 - c. Stop pen VK and initiate Augmentin 500/125 tid or q 8h.
4. Allergy or intolerance to penicillins, cephalosporins, macrolides, clindamycin
 - a. Reserve agents include levofloxacin or moxifloxacin but be aware of toxicities and new warnings.
 - b. May combine fluoroquinolone with metronidazole for resistant anaerobic infections
5. Patient may be pregnant
 - a. Use penicillins, cephalosporins, clindamycin, azithromycin
 - b. Avoid clarithromycin, all fluoroquinolones and tetracyclines

G. APPROACH TO PRESCRIBING ANTIBIOTICS FOR ODONTOGENIC INFECTIONS

1. Establish a clear need for antibiotics

Patient presents with malaise, fever, chills, trismus, rapid respirations, swelling, lymphadenopathy, or hypotension

Signs an sx of infection have escalated rapidly over the past 24 to 48 hours

Oral soft tissue swelling appears to be spreading

Patients presenting with signs of impending airway obstruction, marked trismus

(<25mm), dehydration, malaise, disorientation, tachycardia, and hypotension **SHOULD BE ADMITTED TO THE HOSPITAL** for urgent care.

2. Determine the Patient's Health Status

Systemic Considerations

History of Adverse Drug Reactions

Potential Drug-Drug Interactions

3. Select appropriate agent with narrow spectrum and limited toxicity (if you can)

Immune status of patient determines static vs cidal

Empiric therapy based on most likely organisms associated with odontogenic infections

Culture and sensitivity testing if patient compromised or resistance is suspected

Establish a dosage regimen based on Sanford Guide, Dental Lexi-Drugs, Micromedex, etc

Consider severity and compliance issues

Follow up in 48 hours to check compliance and response to treatment

Monitor patient for adverse effects

Duration of therapy typically 3-5 days post definitive dental treatment

Patient should continue therapy 24 hours past symptom resolution

Antimicrobial Adult Regimens for Odontogenic Infections

PENICILLINS

NAME	USUAL DOSAGES	USUAL REGIMENS
PENICILLIN VK (generic)	Tablet: 250MG, 500MG	500MG TAB QID OR Q 6 HOURS UNTIL GONE.
AMOXICILLIN (generic)	Capsules: 250MG,500MG Tablets: 250MG CHEWABLE Tablets: 875MG	500MG CAP TID OR Q 8 HOURS UNTIL GONE. DON'T USE 875mg BID DUE TO SHORT DURATION.
AMOXICILLIN/POTASSIUM CLAVULANATE (AUGMENTIN,G)	Tablets: 250 mg amoxicillin with 125 mg clavulanate, 500 mg amoxicillin with 125 mg clavulanate, 875 mg amoxicillin with 125 mg clavulanate.	500MG/125MG TID OR Q 8 HOURS UNTIL GONE. DON'T USE 875mg BID DUE TO SHORT DURATION OF AMOXICILLIN

CEPHALOSPORINS

NAME	USUAL DOSAGES	USUAL REGIMENS
Cefaclor (Ceclor, generic)	Capsule: 250 MG, 500 MG Powder for Suspension: 125 MG/5 ML, 187 MG/5 ML, 250 MG/5 ML, 375 MG/5 ML Tablet, Extended Release: 500 MG	250mg-500mg TID OR Q 8 HOURS UNTIL GONE.
Cefuroxime (Ceftin, generic)	Powder for Suspension: 125 MG/5 ML, 250 MG/5 ML Tablet: 125 MG, 250 MG, 500 MG	250mg-500mg BID OR Q 12 HOURS UNTIL GONE.
Cefzil (Cefprozil, generic)	Powder for Suspension: 125 MG/5 ML, 250 MG/5 ML Tablet: 250 MG, 500 MG	250mg-500mg BID OR Q 12 HOURS UNTIL GONE.

MISCELLANEOUS

Clindamycin (Cleocin, generic)	Capsules: 75mg,150mg,300mg Suspension:	150-450mg QID OR Q 6 HOURS UNTIL GONE.
Metronidazole (Flagyl, generic)	Capsules: 375mg Tablets: 250mg, 500mg	1-2 GRAMS DAILY AS: 250MG QID OR 375MG TID OR 500MG TID – QID.

MACROLIDES

Name	Usual Dosages	Usual Regimens
Azithromycin (Zithromax Z-Pak)	Oral Powder for Suspension: 1 GM/Packet, 100 MG/5 ML, 200 MG/5 ML Oral Tablet: 250 MG, 500 MG, 600 MG	500mg on Day 1, followed by 250mg daily for 4 more days.

FLUOROQUINOLONES

Name	Usual Dosages	Usual Regimens
Levofloxacin (Levaquin, generic)	Oral Tablet: 250 MG, 500 MG, 750 MG	250mg-500mg QD UNTIL GONE
Moxifloxacin (Avelox, generic)	Oral Tablet: 400mg	400mg QD UNTIL GONE

Antimicrobial Prescribing for Odontogenic Infections Decision Criteria

1. Assess the nature and severity of the infection
 - a. Small, isolated, non-progressive with no systemic spread
 - i. Definitive dental treatment alone may be adequate
 - b. Large, rapidly progressive with systemic spread
 - i. Definitive dental treatment PLUS antibiotic therapy
2. Assess the patient's immunocompetence
 - a. Immune system normal-static or cidal antibiotic effective
 - b. Immune system suppressed-cidal antibiotic preferred
3. Assess the patient's disease states & corresponding chronic drug therapy
 - a. Any disease interactions with dental antibiotics?
 - b. Any patient drug interactions with dental antibiotics?
4. Antibiotic Selection Based on Above Factors
 - a. First line less aggressive therapy
 - i. Penicillin VK 500mg qid
 - ii. Amoxicillin 500mg tid
 - iii. Azithromycin 500mg, then 250mg daily x 4 days
 - b. First line aggressive therapy for large rapidly progressive infections with signs and symptoms of systemic spread
 - i. Amoxicillin/clavulanate 500mg/125mg tid
 - ii. Penicillin VK 500mg plus metronidazole 250or500mg both qid
 - iii. Clindamycin 300mg qid
 - iv. Moxifloxacin 400mg qd
 - c. Patients at increased risk of CDIC
 - i. Pen VK 500mg plus metronidazole 250-500mg both qid
 - ii. Azithromycin 500mg, then 250mg days 2-5
 - iii. AVOID Amox/clav, Clindamycin, Levofloxacin, Moxifloxacin
 - d. Remember, failure of less aggressive first line therapy indicates proliferation of resistant gram negative anaerobes so make changes to antimicrobial therapy with this in mind. You will need to start or add a drug that is effective against most oral anaerobes. This means starting clindamycin as a single agent or adding metronidazole to the previous failing beta lactam.

Typical duration of antibiotic therapy after definitive treatment is 3-7 days and tell patient to stop the antibiotic when symptom free for 24 hours. This duration is usually about 5 days but may be up to 7 days

AN UPDATE ON ANTIBIOTIC PROPHYLAXIS IN DENTAL PRACTICE

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The University of Iowa© 2026 kbaker

I. ANTIMICROBIAL PROPHYLAXIS: for prevention of infection pre-&postop

A. RISK FACTORS FOR POST-OPERATIVE INFECTIONS:

1. Proportional to the degree of bacterial contamination during surgery – dirty vs. clean surgeries
2. Virulence of the infective organism – HA-MRSA or CA-MRSA?
3. Host factors – immunocompromised? Type I Diabetics

B. TIMING OF PRE- & PERISURGICAL PROPHYLAXIS

IV REGIMENS: Recommend a single dose given just prior to surgery

Give follow-up dose when: drug has short $t_{1/2}$, for prolonged surgeries, ↑ blood loss

PO REGIMENS: Peak plasma concentration of antibiotic should occur when surgery begins

C. SOURCES OF BACTERIAL CONTAMINATION

EXOGENOUS: Due to poor aseptic technique, high O.R. traffic, colonized surgeons

ENDOGENOUS: Flora from patient's skin, GI, GU, or respiratory tract, dirty wounds (pus)

most common cause of post-op infections

D. ANTIMICROBIAL AGENTS-how does a single pre-procedural dose prevent distant site infection?

MECHANISM OF ACTION ??: ↓ Level of bacteremia and bacterial growth after adherence
Prevents adherence of bacteria to defect or prosthetic device

- Direct prophylaxis against the most likely infective organisms:
 - Usually normal skin flora
 - Target specific organisms
- For dental procedures: Coverage of Viridans streptococci
 - Amoxicillin preferred by A.H.A. (American Heart Association) over penicillin VK citing better absorption & more prolonged serum levels

E. PROPHYLACTIC ANTIBIOTICS PRIOR TO IMPLANT PLACEMENT AND IMPLANT FAILURE RATES

Efficacy of preoperative antibiotics in prevention of dental implant failure: a Meta-analysis of randomized controlled trials
Oral Maxillofac Surg 24, 469–475 (2020). <https://doi.org/10.1007/s10006-020-00872-5>

Considering the results of our study, we conclude that preoperative amoxicillin 1 h prior to surgery significantly reduces the rate of implant failure. But, the potential of this conclusion is limited due to various confounding factors, the varied methodologies of the included studies, the difference in surgical techniques, and the difference in patients' data. Furthermore, research is required in the direction where more complicated implant surgeries are conducted like implant placement with maxillary sinus lift, alveolar ridge splits, bone grafting, and soft tissue grafting.

F. ESSENTIAL REFERENCES:

Circulation. 2021;143:e963–e978 (May 2021 J of the AHA Prevention of VGS Endocarditis Guidelines)

J Bone Joint Surg Am. 2017;99:161-3 (January 2017 AAOS AUC App for Joint Replacement Preme)

CID 2020:71 (15 July) (Reviews The History of Antibiotic Prophylaxis and How to Resolve Conflicts)

II. ANTIBIOTIC PROPHYLAXIS FOR PATIENTS WITH TOTAL JOINT REPLACEMENTS

A. GUIDELINES FOR ANTIMICROBIAL PROPHYLAXIS – TIMELINE FROM 2003 THROUGH 2025

- Advisory statement adopted by the ADA and the AAOS (American Academy of Orthopedic Surgeons), published *JADA* 134:895-899, July 2003. AAOS “retired” that advisory statement in February of 2009.
- February 2009 AAOS Information Statement recommends lifelong antimicrobial prophylaxis for all patients with total replacements of large weight-bearing joints even though no new evidence for the change exists.
- *Given this new “Information Statement”, Orthopedic Surgeons now bear prescriptive responsibility if the dentist does not deem premedication to be appropriate. See **Clinical Infectious Diseases**, 1/1/10 and **JADA**; 141:667-671. (Position Paper from the AAOM on Dental Treatment of Joint Patients); Also see *JADA* December 2011.*
- Evidence-based recommendation issued December 18, 2012 with guideline writing committee appointed.

This clinical practice guideline, with three recommendations, is based on a systematic review of the correlation between dental procedures and prosthetic joint infection (PJI).

- Recommendation one, which is based on limited evidence, supports that practitioners consider changing their longstanding practice of prescribing prophylactic antibiotics for patients who undergo dental procedures. Limited evidence shows that dental procedures are unrelated to PJI.
- Recommendation two addresses the use of oral topical antimicrobials (topical antibiotic administered by a dentist) in the prevention of PJI in patients undergoing dental procedures. There is no direct evidence that the use of oral topical antimicrobials before dental procedures will prevent PJI.
- Recommendation three is the only consensus recommendation in the guideline, and it supports the maintenance of good oral hygiene.

B. ADA Constitutes 2014 Committee and Publishes Clinical Recommendations in January 2015

Management of patients with prosthetic joints undergoing dental procedures

Clinical Recommendation:

In general, for patients with prosthetic joint implants, prophylactic antibiotics are **not** recommended prior to dental procedures to prevent prosthetic joint infection.

For patients with a history of complications associated with their joint replacement surgery who are undergoing dental procedures that include gingival manipulation or mucosal incision, prophylactic antibiotics should only be considered after consultation with the patient and orthopedic surgeon.* To assess a patient’s medical status, a complete health history is always recommended when making final decisions regarding the need for antibiotic prophylaxis.

Clinical Reasoning for the Recommendation:

- There is evidence that dental procedures are not associated with prosthetic joint implant infections.
- There is evidence that antibiotics provided before oral care do not prevent prosthetic joint implant infections.
- There are potential harms of antibiotics including risk for anaphylaxis, antibiotic resistance, and opportunistic infections like *Clostridium difficile*.
- The benefits of antibiotic prophylaxis may not exceed the harms for most patients.
- The individual patient’s circumstances and preferences should be considered when deciding whether to prescribe prophylactic antibiotics prior to dental procedures.

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ADA. Center for Evidence-Based Dentistry™

* In cases where antibiotics are deemed necessary, it is most appropriate that the orthopedic surgeon determine the appropriate antibiotic regimen and when reasonable write the prescription.

C. AAOS Appropriate Use Criteria (AUC) for Total Hip and Knee Replacement Patients Undergoing Dental Procedures June 6, 2025 (2 Question App with criteria for immunocompromised status)

We recognize that in the office setting, some specific laboratory values and other patient data are not always readily available. This also may include timely access to published scientific studies that can support clinical decision-making. Appropriate Use Criteria (AUC) specify when it is appropriate to perform a clinical procedure or service. An “appropriate” procedure is one for which the expected health benefits greatly exceed the expected health risks. Ideally, AUC are evidence-based, but in the absence of sufficient evidence, may be derived from a “consensus of expert opinion” and “accepted practice”.

With this AUC, we have attempted to define clinical situations in which antibiotic prophylaxis in certain at-risk dental patients could reduce a theoretical risk of post-surgical prosthetic joint infection. This AUC was developed as a decision support tool to facilitate the treatment of defined “high risk” and “immune compromised” patients who are on the more severe end of the clinical spectrum of disease. In the absence of readily available laboratory data or suggestive clinical suspicion, it would be reasonable to assume that most patients will fall outside of these criteria and therefore lay outside the confines of our strict definitions. As always, sound judgment should guide clinical decisions about when it may be necessary or prudent to delay a dental procedure until more information is available.

Assumptions:

Planned Dental Procedures

- The chance of oral bacteremia being related to joint infections is extremely low, with no evidence for an association.
- Oral bacteremia frequently occurs secondary to activities of daily living such as tooth brushing and eating.
- Virtually all dental office procedures have the potential to create bacteremia.

Immunocompromised Status

1. Severely immunocompromised patients include:
 - a. Patient with Stage 3 AIDS as defined by the Centers for Disease Control and Prevention (CDC) Guidelines when the immune system becomes severely compromised due to reduced CD4 T lymphocyte counts (<200) or opportunistic infection as defined by CDC⁸ see list of diseases below.
 - b. Cancer patient undergoing immunosuppressive chemotherapy with febrile (Celsius 39) neutropenia (ANC <2000) OR severe neutropenia irrespective of fever (ANC <500)
 - c. Rheumatoid arthritis with use of biologic disease modifying agents including tumor necrosis factor alpha or prednisone >10 mg per day. Methotrexate, Plaquenil not considered immunocompromising agents.
 - d. Solid organ transplant on immunosuppressants
 - e. Inherited diseases of immunodeficiency (e.g., congenital agammaglobulinemia, congenital IgA deficiency)
 - f. Bone marrow transplant recipient in one of the following phases of treatment:
 - i. Pretransplantation period
 - ii. Preengraftment period (approximately 0-30 d posttransplantation)
 - iii. Postengraftment period (approximately 30-100 d posttransplantation)
 - iv. Late posttransplantation period (≥100 d posttransplantation) while still on immunosuppressive medications to prevent GVHD (typically 36 months post transplantation) (see Table reference below)

*Opportunistic illness in AIDS: (as per CDC⁶)

Glycemic Control

1. A1C scores should be recent within 3-6 months.
2. Acucheck spot check in dental office blood glucose level is equivalent to a patient self-report.
3. Blood glucose tests are assumed to be random (not necessarily fasting).
4. Every Dental Office should be able to take an ambient blood glucose or HgA1c Chairside.

Definitions of Invasive vs Non-Invasive Dental Procedures per AAOS 2025

1. Level of Invasiveness

NON-INVASIVE

- Dental examination without probing dental radiograph or cone beam CT imaging, denture adjustment procedures, clear orthodontic aligner (invisible braces) adjustment procedures, occlusal guard or bite splint adjustment
- Oral hygiene procedures including dental cleaning, dental prophylaxis using a rubber cup and handpiece [without scaling] or periodontal probing (without SRP)
- Orthodontic procedures including banding or debanding orthodontic fixes or removable appliances, archwire adjustment, orthodontic mini-implant removal, orthodontic separate placement
- Other non-invasive procedures including suture removal, anesthetic injection, crown and bridge placement, dental restorative procedures, rubber dam clamp or matrix band wedge between teeth, impression taking, endodontic treatment (root canal therapy).

INVASIVE

- Scaling and/or root planing (SRP) with manual (hand instruments) or ultrasonic scaler
- Dental Extractions including single, multiple, impacted third molar
- Oral Surgery (including dental implant surgery, periodontal surgery, cleft palate surgery, piezoelectric surgery, osteosynthesis plate removal)
- Treatment of Active Dental Infection

APPROPRIATE USE CRITERIA: MANAGEMENT OF PATIENTS WITH ORTHOPAEDIC IMPLANTS UNDERGOING DENTAL PROCEDURES (2025)

Endorsed by: MSIS

INDICATION PROFILE

Level of Invasiveness of Dental Procedure ?

- Non-Invasive - Dental procedures that do not result in the manipulation of gingival or periapical tissues, or perforation of the oral mucosa
- Invasive - Dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa

Systemic Host Status

- Immunocompetent
- Immunocompromised

PROCEDURE RECOMMENDATIONS

SUBMIT

D. AAOS Evidence-Based Clinical Practice Guideline Adopted November 24, 2024

1. USE OF ANTIBIOTIC PROPHYLAXIS BEFORE DENTAL PROCEDURES

- AAOS-AAHKS guideline now agrees with ADA 2015 guideline stating there is no association between invasive dental procedures and late prosthetic joint infections (LPJIs), and that antibiotic prophylaxis is of no benefit.
- AAOS-AAHKS states, "Routine use of a systemic prophylactic antibiotic prior to a dental procedure in patients with a hip or knee replacement may not reduce the risk of a subsequent periprosthetic joint infections."
- COMMENTS:** These guidelines pertain to primary joint replacement patients. Some stakeholders are concerned about higher risk patients such as revision TJA, prior PJI or immunocompromised patients (see CDC criteria for immunocompromised status on previous page 3).

2. **DENTAL SCREENING BEFORE HIP OR KNEE ARTHROPLASTY**
 - a. AAOS-AAHKS guideline acknowledges there is no evidence that dental screening or clearance before Arthroplasty reduces the risk of prosthetic joint infections.
 - b. **COMMENTS:** Consensus opinion supports optimization of dental hygiene prior to elective TJA.
3. **USE OF AN ANTISEPTIC MOUTHRINSE BEFORE DENTAL PROCEDURES**
 - a. AAOS-AAHKS guideline acknowledges there is no evidence to support the use of an antiseptic Mouthrinse before invasive dental procedures.
 - b. **COMMENTS:** Some small studies show reduction in magnitude and range of bacteria after rinsing With chlorhexidine 15ml for 1 minute prior to invasive dental procedures.
4. **TIMING OF ARTHROPLASTY SURGERY AFTER ANY DENTAL PROCEDURE**
 - a. AAOS-AAHKS guideline recommends delaying arthroplasty surgery for 1 week after SRP and for 3 weeks after an extraction, oral surgical procedure, or treatment of an acute dental infection.
 - b. **COMMENTS:** Oral epithelization takes about three weeks after oral surgical procedures so that's the basis for the 3 week delay before arthroplasty. Non-invasive or minimally invasive dental procedures can be performed up to one day prior to arthroplasty.
5. **TIMING OF ANY DENTAL PROCEDURE AFTER TOTAL JOINT ARTHROPLASTY**
 - a. AAOS-AAHKS guideline recommends delaying any invasive dental treatment other than emergent care for three months after joint replacement surgery.
 - b. **COMMENTS:** The ADA disagrees with this recommendation because it may limit timely dental care. Planning elective dental treatment to accommodate elective TJA is a good option here.

E. PRESCRIPTIONS FOR PATIENTS WHO MIGHT BENEFIT FROM ANTIBIOTIC PROPHYLAXIS

Rx: Amoxicillin 500 mg capsules

or

Cephalexin 500 mg capsules

Disp: # 4

Sig: Take 4 capsules p.o. 1 hr. prior to dental appointment

- Amox Is for patients **NOT** allergic to penicillin

- Cephalexin is a 1st generation cephalosporin with good strep. coverage and active against staphylococcal organisms

Rx: Azithromycin 250mg tablets

Disp: # 2

Sig: Take 2 tablets p.o. 1 hr. prior to dental appointment

Rx: Cefazolin 1 gram or Ampicillin 1 gram

Administer: I.M. or I.V.

Sig: 1 hr. prior to procedure

- For patients unable to take oral medications AND NOT allergic to penicillin

Rx: Ceftriaxone 1 gram

Administer: I.V. or I.M.

Sig: 1 hr. prior to procedure

- For patients unable to take oral medications AND penicillin allergic

-Give IM injection with lidocaine 1% solution added

F. BEST PRACTICES FOR DENTAL MANAGEMENT OF PATIENTS WITH TOTAL JOINT REPLACEMENTS

- ◆ Updated health history with each visit and explain why you ask at every visit
- ◆ Reinforce home-care procedures and use chemotherapeutic measures to reduce bleeding
- ◆ Immediate and aggressive treatment of acute and newly recognized chronic infections
- ◆ Avoidance of regular daily bacteremia

2021 AHA Guidelines for the Prevention of Infective Endocarditis

A. Regimens for a Dental Procedure

Situation	Agent	Regimen – Single dose 30-60 minutes before procedure	
		Adults	Children
Oral	Amoxicillin	2 g	50 mg/kg
Oral Allergic to penicillins or ampicillin	Cephalexin**† OR	2 g	50 mg/kg
	Azithromycin OR	500 mg	15 mg/kg
	Doxycycline	100 mg	<45kg – 2.2mg/kg
Unable to take oral medication	Ampicillin OR	2 g IM or IV*	50 mg/kg IM or IV
	Cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillins & unable to take oral med	Cefazolin or ceftriaxone†	1 g IM or IV	50 mg/kg IM or IV

*IM – intramuscular; IV – intravenous.

**or other first or second generation oral cephalosporin in equivalent adult or pediatric dosage.

†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin

B. AP for a Dental Procedure Underlying Conditions for Which AP is Suggested (Table 3.)

Prosthetic cardiac valve or material

Presence of cardiac prosthetic valve

Transcatheter implantation of prosthetic valves

Cardiac valve repair with devices, including annuloplasty, rings, or clips

Left ventricular assist devices or implantable heart

Previous, relapse, or recurrent IE

CHD

Unrepaired cyanotic congenital CHD, including palliative shunts and conduits.

Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by transcatheter during the first 6 mo after the procedure

Repaired CHD with residual defects at the site of or adjacent to the site of a prosthetic patch or prosthetic device

Surgical or transcatheter pulmonary artery valve or conduit placement such as Melody valve and Contegra conduit

Cardiac transplant recipients who develop cardiac valvulopathy

C. AP for a Dental Procedure IS NOT RECOMMENDED (Table 3.)

Implantable electronic devices such as a pacemaker or similar devices
 Septal defect closure devices when complete closure is achieved
 Peripheral vascular grafts and patches, including those used for hemodialysis
 Coronary artery stents or other vascular stents
 CNS ventriculoatrial shunts
 Vena cava filters
 Pledgets

D. Dental Procedures for which Antibiotic Prophylaxis is Recommended for Patients

All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa *

***The following procedures and events do not need prophylaxis:** routine anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of primary teeth and bleeding from trauma to the lips or oral mucosa.

E. SAMPLE ADULT ANTIBIOTIC PREMEDICATION PRESCRIPTIONS

RX: Amoxicillin 500 mg capsules

Disp. # 4

Sig: Take 4 capsules p.o. 1 hour before dental Appointment

- **For patients NOT penicillin allergic**

- Pediatric dose: 50 mg/kg not to exceed adult dose!

- Amoxicillin is available in 500 and 250 mg **capsules**, and 250 mg chewable tablets and 250 mg/5 ml susp.

RX: Cefaclor 500 mg capsules

Disp. # 4

Sig: Take 4 capsules p.o. 1 hour before dental appointment

- Pediatric dose: 50 mg/kg

- Cefaclor (generic Ceclor®) is second generation ceph

- Also comes in a 250 mg/5ml suspension

- Avoid ALL cephalosporins if patients allergic reaction was either – urticarial, angioedema, anaphylaxis or unknown

RX: Azithromycin (Zithromax®) 250 mg tablets

Disp. #2

Sig: Take 2 tablets p.o. 1 hour before appointment.

- Pediatric dose: 15 mg/kg

- Less drug interactions than macrolides, low incidence of GI irritation

Oral liquids for adults who have forgotten to take AP at home:

RX: Amoxicillin 250 mg/5 ml suspension

Disp. # 40 ml

Sig: Take 40 ml one-half to one hour before dental appointment

- Suspension is a powder that must be reconstituted prior to use- tastes good

- Reconstituted suspension expires in 14 days with or without refrigeration. Tastes good!

RX: Azithromycin 200 mg/5 ml susp.

Disp. # 15 ml (pour out 12.5ml for 500mg)

Sig: Take 12.5 ml one-half hour before dental appointment

- Suspension is commercially available as 600mg/15ml

- 12.5ml is 500mg of azithromycin

- Tastes good!

V. OTHER CONDITIONS THAT MAY REQUIRE ANTIMICROBIAL PROPHYLAXIS

A. SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

BACKGROUND:

- SLE is an inflammatory autoimmune disease whereby pathogenic antigen-antibody complexes harm a variety of organs & systems including the skin, kidneys, blood vessels, joints and the heart
- 50% of SLE patients demonstrate cardiac valve abnormalities at autopsy
- SLE patients have an increased prevalence of cardiovascular abnormalities
- **Incidence of Infective Endocarditis:** SLE = 1 - 7%
RHD = 0.8 - 1.2%
Prosthetic heart valve = 1.1%

MANAGEMENT: *Progressive SLE patients should be regularly evaluated for the detection of new heart murmurs
And patients should be questioned about cardiac valve disease at dental visits.*

B. ASPLENIC PATIENTS

BACKGROUND (*JADA: Dental Considerations in Asplenic Patients. 127:1359-1363, 1996*)

- Patients who are functionally or anatomically asplenic fail to clear organisms from the bloodstream and are at an increased risk of overwhelming bacteremia
- Reasons for splenectomy
- Encapsulated organisms pose the highest risk - primary pathogens of concern are *S. pneumoniae*, *H. influenzae*, *N. meningitidis*, β - hemolytic streptococci
- Splenectomy confers life-long risk from sepsis in both adults and children (2 - 4%)
- Recommend dental prophylaxis with current AHA regimen when needed
-

C. SOLID ORGAN TRANSPLANTATION

BACKGROUND: (*Clin Transplant. A Survey of Dental Care Protocols. 19: 15-18, 2005*)

- Infectious Disease Rates of Patients
 - 80% have "normal" rate of infections
 - 10% chronic or progressive viral infections
 - Hepatitis B or C, cytomegalovirus, EPV etc.
- Theoretically at ↑ risk from transient bacteremias
- 5-10% recurrent or chronic rejection
 - Increased immunosuppressive dosages (tacrolimus, mycophenolate, prednisone)
 - Most likely to develop opportunistic infections

MANAGEMENT:

- Defer elective dental treatment until at least 6 months after transplantation

D. CORONARY ARTERY STENTS

The report published in *JADA* can be summarized for the dental professional as follows:

1. Dental professionals and other healthcare providers who perform invasive or surgical procedures and are concerned about periprocedural and postoperative bleeding must be made aware of the potential catastrophic risks of premature discontinuation of antiplatelet (thienopyridine) therapy. The dental professional should contact the patient's physician if issues regarding the patient's antiplatelet therapy are unclear, in order to discuss optimal patient management strategy.
2. Elective procedures for which there is significant risk of perioperative or postoperative bleeding should be deferred until patients have completed an appropriate course of thienopyridine therapy. The course of this therapy is suggested as 12 months after drug-eluting stent implantation if they are not at high-risk of bleeding.

WHAT ABOUT ANTIBIOTIC PREMEDICATION?? According to the 2021 AHA guidelines, antibiotic prophylaxis is not indicated as stated in previously listed Table 3.

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. VETERANS HEALTH ADMINISTRATION ACUTE PAIN LADDER

Managing Acute Pain Safely and Effectively²

To manage acute pain safely and effectively, first evaluate the severity of the pain based on the evaluation of the patient, diagnosis, and the patient's feedback about the pain and impact of the pain on their functioning.

Figure 4. Step-wise Approach to Acute Pain Management²



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.

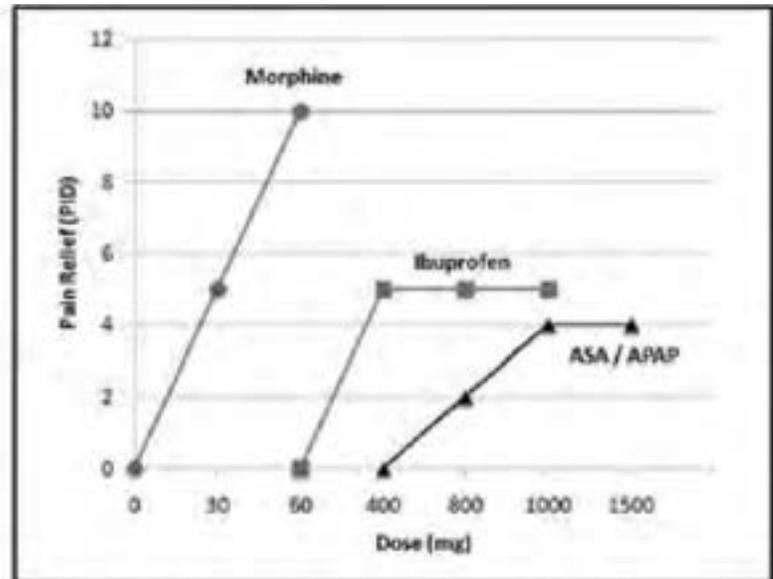


Figure 2. Analgesic efficacy. This graph illustrates a typical dose-response curve for orally administered (PO) analgesics. The dose-response curve for opioids such as morphine demonstrates unlimited efficacy in which greater doses provide greater analgesia. At equipotent doses, all opioids demonstrate 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 +/- ELDERLY PATIENT:* Maximum of 2.6 grams APAP/day

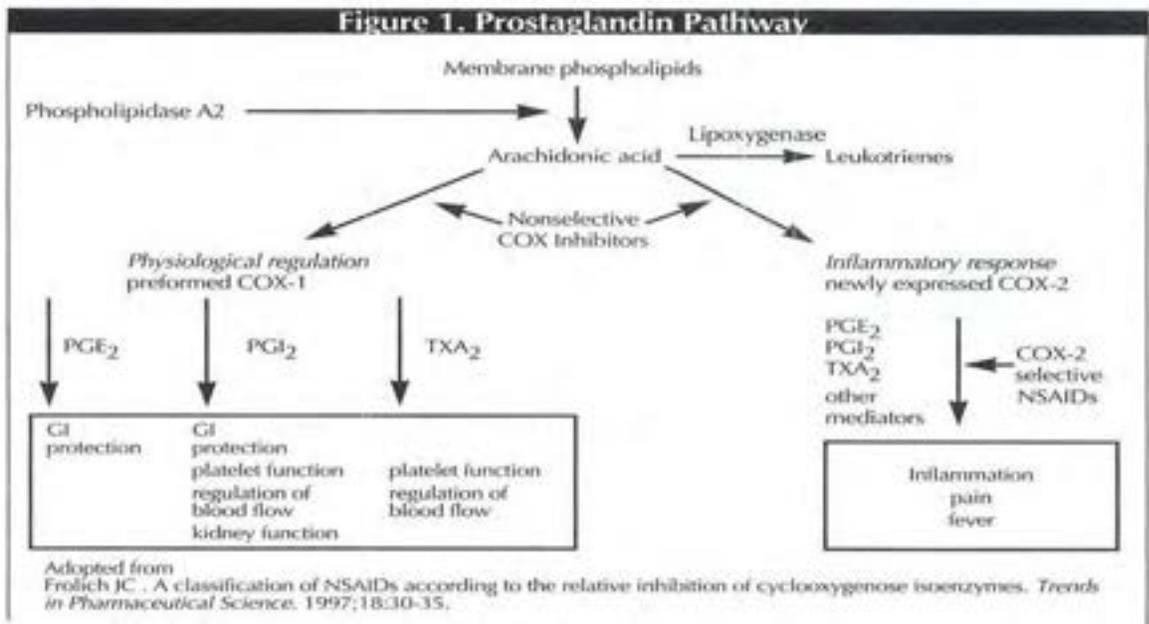
<u>PRODUCT</u>	<u>DOSAGE</u>	<u>ACUTE</u>	<u>CHRONIC</u>
Regular Strength APAP	325mg	12/day	8/day
Extra Strength APAP	500mg	8/day	5/day
Extended Relief APAP	650mg	6/day	4/day

Toxicity risk is increased by:

- *Fasting (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 *	T_p (hr)	t 1/2 (hr)	ANALGESIC Onset (hr)	ANALGESIC Duration (hr)	USUAL ADULT DOSE (mg)	MAX. DAILY DOSE (mg)
<u>PROPRIONIC ACIDS</u>							
<i>ibuprofen (Motrin,G,otc)</i>	P	1-2	1.8-2.	.5	4-6	400-600 q4-6h	3200/1200
<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>ENOLIC ACIDS</u>							
<i>Meloxicam (Mobic,G)</i>	P	5	20-26	4	up to 24	5-15mg once daily	15
<i>Piroxicam (Feldene,G)</i>	P	5	50	4	up to 48	10-20mg once daily	20
<u>SALICYLATE</u>							
<i>diflunisal (Dolobid,G)</i>	P,I	2-3	8-12	1	8-12	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
 - pre procedural dosing of ibuprofen 400mg or naproxen sodium 275mg reduces postop pain

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 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 → → 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

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. 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	2D ₆ 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 2D ₆ inhibitors*)	0.1	1	3-4	2D ₆ 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

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:

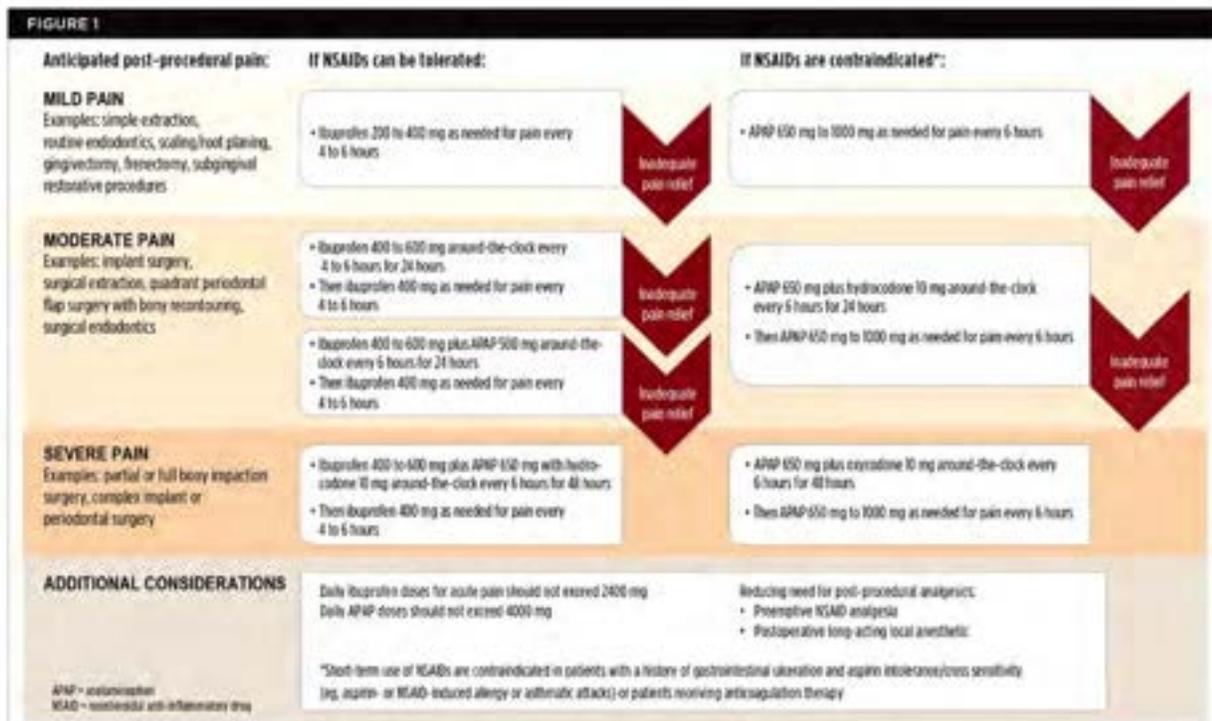
- ✓ Generalized flushing, itching, sweating
- ✓ Mild hypotension accompanied by nausea and/or vomiting
- ✓ Itching, flushing, or hives at injection/application site

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*

Mana Saraghi, DMD; Elliot V. Hersh, DMD, MS, PhD; Victor M. Badner, DMD, MPH; and Nadia Laniado, DDS, MPH



Managing Postoperative Pain in Pediatric Dentistry

Decisions in Dentistry, November 2018; 4(11):32, 35-37.

TABLE 1. Common Medications Used in Children for Mild-to-Severe Postoperative Pain

Analgesic	Pediatric Oral Dosage Children < 12 years (Daily Maximum)	Indication(s)	Caution(s)
Mild-to-Moderate Pain (Examples: Dental procedures, such as restorations, stainless steel crowns, and extractions.)			
Ibuprofen	4–10 mg/kg q6–8h; maximum single dose is 400 mg (40 mg/kg/day)	First-line choice for pain caused by routine dental procedures	Asthmatics, gastric irritant, renal toxicity, liver dysfunction, bleeding (may impair clotting)
Acetaminophen	10–15 mg/kg q4–6h (90 mg/kg/day; not more than five doses/day)	Used for individuals who cannot use an nonsteroidal anti-inflammatory drugs (pregnancy and asthmatics)	Hepatotoxicity
Naproxen Sodium	5–6 mg/kg q12h (1000 mg/day)	While not a typical first-line agent, the longer duration of action may make compliance easier for some patients	Same cautions as those for ibuprofen; over-the-counter instructions will say the medication is for children ≥ 12 years
Moderate-to-Severe Pain (Example: Full-mouth rehabilitation performed under general anesthesia.)			
Ibuprofen and Acetaminophen Combination	Ibuprofen: 4–10 mg/kg q6h Acetaminophen: 10–15 mg/kg q6h	Alternate each medication every three hours and administer for the first 36–48 hours after surgery	The same cautions listed above for ibuprofen and acetaminophen
Acetaminophen With Oxycodone	0.05–0.1 mg/kg/dose of oxycodone Typically, only two to four doses are prescribed for breakthrough pain; maximum doses are limited by daily maximums of acetaminophen	Prescribed for break-through pain; the decision to use this medication may be made in consultation with the patient's primary care physician	In general, opioids are not recommended for children under 12 years of age

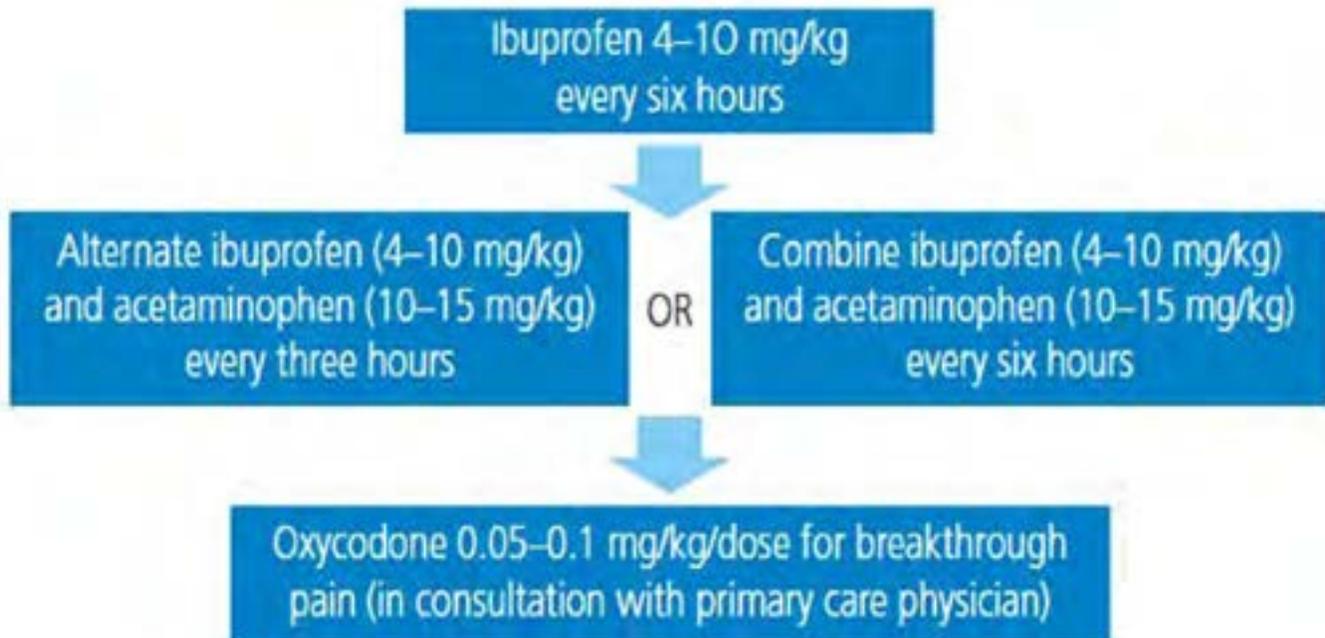


FIGURE 1. Analgesics should be administered around the clock for the first 36–48 hours.

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	11 mg/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 (max 120mg/day)	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.	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



Pharmacological Management of Acute Endodontic Pain

Asma A. Khan¹ · Anibal Diogenes¹

(a)	Pain Intensity	Low	Moderate	Severe
		EXAMPLE A		
	Drugs Prescribed 1-2 days prior to treatment visit and 2-3 days Post-treatment	Ibuprofen (200 to 400 mg) <u>4x day</u>	Ibuprofen (600 mg) + Acetaminophen (500 mg) <u>Both 4x day</u>	Ibuprofen (600 mg) + Acetaminophen (500mg)/ Tramadol (50-100mg) <u>Both 4x day</u>
		EXAMPLE B		
	Drugs Prescribed 1-2 days prior to treatment visit and 2-3 days Post-treatment	Naproxen (320 mg) <u>2x day</u> Acetaminophen (325mg) <u>4x day</u>	Naproxen (440mg) <u>2x day</u> + Acetaminophen (500 mg) <u>4x day</u> Acetaminophen (500mg) <u>4x day</u>	Naproxen (440mg) <u>2x day</u> + Acetaminophen (500mg) / Tramadol (50-100mg) <u>Both 4x day</u> Acetaminophen (500mg) + Tramadol (50mg a 100mg) <u>All 4x day</u>
(b)	Pain Intensity	Low	Moderate	Severe
Drugs Prescribed 1-2 days prior to treatment visit and 2-3 days post-Post-treatment		Acetaminophen (325mg) <u>4x day</u>	Acetaminophen (500mg) <u>4x day</u>	Acetaminophen (500mg) + Tramadol (50mg a 100mg) <u>All 4x day</u>

Fig. 3 a Flexible prescription plan that could be implemented for patients with no contraindication for NSAIDS including two examples or alternative prescriptions for patients presenting with mild, moderate or severe pain. The plan can be initiated pre-operatively and extend to a minimal of 2–3 days post-treatment. Patient must be instructed to take the medications “by the clock as prescribed” (not

“as needed”). **b** Flexible prescription plan that could be implemented for patients with contraindication for NSAIDS but without restrictions related to the use of Acetaminophen. The plan can be initiated pre-operatively and extend to a minimal of 2–3 days post-treatment. Patient must be instructed to take the medications “by the clock as prescribed” (not “as needed”)

Topical and Transdermal Medications*

Class	Formulations (generic & OTC)	Indications	Recommended Dosing
Counterirritants & Rubefacients (cream, lotion, gel, ointment, spray, & patch)	Numerous OTC formulations & varying combinations of camphor, salicylates, and/or menthol (Ex: BENGAY®, Biofreeze®)	Musculoskeletal pain: strains, sprains, backache	Generally, > 12 yo: Apply thin layer to affected area and massage up to QID Check labeling for age cutoff
Captsachin <1% (alone or in combination with other products)	Available as multiple OTC formulations +/- camphor or menthol (Ex: Theragen®, Zostrix®, Tiger Balm®)	Musculoskeletal pain: strains, sprains, backache Post-herpetic neuralgia Peripheral neuropathy	Max 2 patches/day X 3 consecutive days Q 8-12 h
NSAIDs: Diclofenac Combining topical and oral NSAIDs not recommended	Pennsaid®* 1.5% solution 2% solution pump Voltaren 1% gel (OTC- 2 g-2.25 in, see package dosing card) Factor®* 1.3% patch	Osteoarthritis Osteoarthritis	*Pediatric dosing unavailable for Pennsaid 1.5%: 40 drops QID 2 pumps (40 mg) BID to affected knee/joint 2 g upper extremity QID (max 8 g/day) 4 g lower extremity QID (max 16 g/day) 32 g/day max all joints
Lidocaine (Available formulations influx due to supply chain issues)	5% patch (Lidoderm®) 4% patch (+/- menthol, OTC) 4% lotion, spray, etc. (OTC) 4% L.M.X.4® cream (OTC) Onset 30 min; Duration 60 min 2% gel/jelly 5% ointment J-Tip™ with buffered lidocaine (https://tip.com/)	Post-herpetic neuralgia Musculoskeletal pain Burns, cuts, insect bites Burns, cuts, insect bites, venipuncture, LP, abscesses & D Catheter/NG tube insertion; stomatitis IV starts: Onset 1-3 min	Adults: q 12 h, max 3 patches at one time Adults and children ≥ 12 yo: q 12 h ≥ 2 years: TID - QID Apply in area <100 cm² if < 10 kg; < 600 cm² for 10-20 kg — —
Lidocaine combinations (use gloves, EMLA-cover with occlusive dressing, LET-cover with cotton ball & tape)	EMLA® (2.5% Lidocaine 2.5% Prilocaine); Onset 60 min; Duration 3-4 h; Max appl. = 1 h if <3mo/5 kg; otherwise 4 h LET (4% Lidocaine, 1.2:000 Epiinephrine, 0.5% Tetracaine) gel or liquid; Onset 10 min; Duration 30-60 min	Dermal analgesic of intact skin (abscess 1 & D, LP, etc.) Wound repair (non-mucosal)	< 3 mo (< 5 kg): up to 1 g on 10 cm² area; 3-12 mo (> 5 kg): up to 2 g on 20 cm²; 1-6 yo (> 10 kg): up to 10 g on 100 cm²; 7 yo - adult (> 20 kg): up to 20 g on 200 cm² 3 mL (not to exceed maximal lidocaine dosage of 3-5 mg/kg)
Vapococcolant	Pain-Ease®	Cooling intact skin, mucus membranes and minor open wounds	Spray 4-10 sec from distance of 8-18 cm. Stop when skin turns white. Use with caution in children < 4 yo

*Posages are guidelines to avoid systemic toxicity in patients with normal intact skin and with normal renal and hepatic function. Use gloves to apply and/or wash hands after application. Use with caution in children and older adults with thin skin.

Patient Resources

Patient Education & Activity Book

Educational Brochures, Videos, OTC Topical & Oral Medications



Pediatric Pain & Fever Dosing Guide (Liquid)



Visit PAMI's website for more information including naloxone: <https://pami.emergency.med.iax.ufl.edu/>

Funding and Disclaimer Statement

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Updated May 28, 2024



Pain Management & Dosing Guide™

*See disclaimer. Dosages and opioid conversions cannot account for differences in genetics and pharmacokinetics. Common available formulations included.

PAMI materials are free to access and adaptable to your institution.

Contact: PAMI@jax.ufl.edu | 904-244-4986 | @ufpami

Opioid Prescribing and Equianalgesic Chart (based upon 2019 ASHP recommendations*)

Weight risk/benefit in special populations (older adults, renal/hepatic impairment, pregnancy, and lactation)

Generic (Brand)	Onset (O) and Duration (D)	Approximate Equianalgesic Dose*	Recommended STARTING dose for ADULTS	Recommended STARTING dose for CHILDREN (< 6 mo) †
All CII except Tramadol				
Fentanyl (Sublimaze®)	Oral	IV	Oral	IV
	—	—	—	—
	O: <1 min D: 30-60 min	150 mcg (0.15 mg)	50 mcg q 1-2 h	1-2 mcg/kg q 1-2 h (max 50 mcg/dose)
Fentanyl Patch (Duragesic®)	Transdermal patch	Transdermal patch	Do not use in opioid naive pt.	Do not use in opioid naive pt.
	O: 12-24 h; D: 72 h	12.5 mcg	opioid naive pt.	opioid naive pt.
Hydrocodone/APAP 325 mg (5, 7.5, 10 mg tablets) (7.5 mg/325 mg per 15 mL)	O: 30-60 min D: 4-6 h	25 mg	5-10 mg q 4-6 h	0.15 mg/kg Hydrocodone q 4-6 h
Hydromorphone (Dilaudid®) (2, 4, 8 mg tablets)	O: 30 min D: 3-4 h	5 mg	2-4 mg q 4-6 h	0.06 mg/kg q 4-6 h
Methadone (Dolophine®) (15, 30 mg tablets 5 mg/5 mL)	O: 30-60 min D: 6-8 h	Variable	2.5 mg q 8-12 h	0.7 mg/kg/day PO/SC/IM/IV Divided q 4-6 h pm
Morphine (MIRAP®) (15, 30 mg, 10 mg/5 mL)	O: 30-60 min D: 3-5 h	25 mg	5-10 mg q 4-6 h	0.3 mg/kg q 4 h
Morphine ER (MASCOTIN®) (15, 30, 60, 100 mg)	O: 2 h D: 8-24 h	25 mg	2-4 mg q 8 or q 12 h	—
Oxycodone (5, 10, 15, 20, 30 mg tablets)	O: 10-15 min D: 3-6 h	20 mg	5-10 mg q 4-6 h	0.05-0.15 mg/kg q 4-6 h
Oxycodone/325 APAP (Percocet®) (5, 7.5, 10 mg)	O: 1 h D: < 12 h	20 mg	4 Dosed q 12 h	Xampaza ER® not approved for <18 yo
Oxycodone (Xampaza ER®) (9, 13.5, 18, 27, 36 mg caps) (Oxycontin®)	O: 1 h D: < 12 h	20 mg	4 Dosed q 12 h	—
Tapentadol (Nucynta®) (50, 75, 100 mg)	O: 30 min D: 4-6 h	100 mg	50-100 mg q 4-6 h	—
Tramadol (CIV) (50, 100 mg)	O: 1 h D: 3-6 h	120 mg	50-100 mg q 6 h	—

Note: For Buprenorphine, refer to current national guidelines or your local pain specialty service.

†Dosing for extended release (ER) products individualized based on short acting MME.

‡Do not exceed adult dosage when calculating pediatric medications in dose per kg.

Non-opioid Analgesics*

Generic (Brand)	Adult	Pediatric (<12 yo)
Acetaminophen (Tylenol®)	325-650 mg PO q 4-6 h. Max: 4 g/day	15 mg/kg PO q 4-6 h. Max: 75 mg/kg/day
Acetaminophen IV	1 g IV q 6 h pm pain or 650 mg q 4 h	<50 kg: 15 mg/kg IV q 6 h or 12.5 mg/kg IV q 4 h Max: 75 mg/kg/day
Use only if not tolerating PO		
Celecoxib (Celebrex®)	100-200 mg PO daily to q 12 h. Max: 400 mg/day	≥ 2 yo to adult: 10-25 kg: 50 mg PO BID; > 25 kg: 100 mg BID
Diclofenac	50-75 mg PO q 8-12h; 50 mg packet in 30-60 mL H ₂ O	10 mg/kg PO q 6 to 8 h. Max: 40 mg/kg/day or 2400 mg/day
Ibuprofen (Motrin®)	400-800 mg PO q 6 to 8 h. Max: 3200 mg/day	0.5 mg/kg IV/IM q 6 h up to 72 h Max: 30 mg/dose IM, 15 mg/dose IV
Ketorolac (Toradol®)	15 mg IV or 15-30 mg IM q 6 h	—
Meloxicam (Mobic®)	30mg IV daily; 7.5-15 mg PO daily	≥ 2 yo 0.125 mg/kg/dose. NTE adult dose Max: 1000 mg/day
Naproxen (Naprosyn®)	250-500 mg PO q 12 h	—
Lidocaine for renal colic†	1.5 mg/kg/IV in 100 mL NS over 10-15 min. Max 200 mg	—

*Avoid NSAIDs in renal/hepatic impairment, PUD, CHF, < 6 mo of age, >20 wks pregnant. Use with caution in age > 65 yo, and those with cardiovascular risks. Give with food. For pediatrics, do not exceed adult dosage.

†Cardiac monitoring preferred. Contraindications: Pregnancy, cardiac arrhythmias, CAD, age > 65 yo, hepatic/renal failure, epilepsy, amide allergy.

Opioid Cross-Sensitivities

Phenanthrenes (related to morphine)	Morphine, Codeine, Oxycodone, Hydrocodone, Hydromorphone
Phenylpiperidines (related to meperidine)†	Meperidine, Fentanyl

Risk of cross-sensitivity in patients with allergies increases when medications from the same opioid family are administered. Itchy, nausea, vomiting are not opioid allergies.

Procedural Sedation and Analgesia Medications

Generic (Brand)	Adult	Pediatric	Comments
Dezme- detomidine (Precedex®)	IV 1 mcg/kg loading dose (over 10 min) followed by 0.5 to 2 mcg/kg/h continuous infusion. Use 0.5 mcg/kg for geriatric patients.	IV 0.5–2 mcg/kg loading dose (over 10 min) followed by 0.5 to 2 mcg/kg/h continuous infusion IN 2-3 mcg/kg	Risk of bradycardia, hypotension, especially with loading dose or rapid infusions, apnea, bronchospasm, respiratory depression
Etonitdate (Amidate®)	IV 0.1–0.2mg/kg; additional doses 0.05mg/kg		Risk of myoclonus (premedication w/ benzos or opioid can decrease), pain with injection, nausea or vomiting, risk of adrenal suppression. Provides no analgesia. 100 times more potent than morphine. Rapid bolus infusion may lead to chest wall rigidity. Reduce dosing when combined with benzodiazepines and in elderly. Preferred agent due to rapid onset and short duration.
Fentanyl	IV 0.5-1 mcg/kg (slow push)	1-3 yo: 2 mcg/kg; 3-12 yo: 1-2 mcg/kg	
Ketamine (Ketalar®)	IV 0.5-1 mg/kg (slow push) IM 4-5 mg/kg	>3 mo: IV 1-2 mg/kg; additional doses 0.5 mg/kg; IV q 10-15 min prn; IM 4- 5 mg/kg	Small risk of laryngospasm increases with active asthma, URI and procedures involving posterior pharynx. Vomiting is common, consider pre-treatment with anti-emetic. Not recommended in patients <3 mo.
Ketamine + Propofol	—	IV ketamine 0.75 mg/kg + propofol 0.75 mg/kg. Additional doses: ketamine 0.5 mg/kg, propofol 0.5-1 mg/kg	See Ketamine and Propofol comments. Recommend against mixing propofol + ketamine in the same syringe.
Midazolam (Versed®)*	IV 0.05-0.1 mg/kg IV slow push over 1-2 min	IV 0.05-0.1 mg/kg IN 0.2-0.3 mg/kg (IN max 10 mg)	Initial max dose 2 mg. Max total dose in >60 yo is 0.1 mg/kg. Decrease dose by 33-50% when given with opioid.
Morphine	IV 0.05-0.1 mg/kg or 5-10 mg	IV 0.1-0.2 mg/kg, titrated to effect	Monitor mental status, hemodynamics, and histamine release. Requires longer recovery time than fentanyl. Difficult to titrate during procedural sedation due to slower onset and longer duration of action. Reduce dosing when combined with benzodiazepines (combination increases risk of respiratory compromise).
Propofol (Diprivan®)*	IV 0.5-1 mg/kg slow push (1-2 min); Additional doses 0.25-0.5 mg/kg over 1-3 min	IV 1 mg/kg slow push (1-2 min); Additional doses 0.5 mg/kg	Risk of apnea, hyperventilation, respiratory depression, rapid changes in sedative depth, hypotension. Provides no analgesia.

*No analgesic properties for Propofol and Midazolam.

Indications	Ketamine (Ketalar®)	
	Starting Dose	
Procedural Sedation	IV: <u>Adult</u> 0.5-1 mg/kg; <u>Pediatric</u> 1-2mg/kg; IM: 4- 5 mg/kg	
Sub- dissociative Analgesia	IV: 0.1 to 0.3 mg/kg IM: 0.5-1 mg/kg; IN: 0.5-1 mg/kg	
Agitated Delirium	IV: 1 mg/kg; IM: 4- 5 mg/kg	
Infusions for Pain	IV: 0.1 - 0.5 mg/kg/hr	

†Consider in opioid tolerant patients or those with contraindications to opioids. Administer IV over 10-15 minutes to minimize side effects. SQ dose same as IV. For IV-can dilute dose in 10 mL NS and administer as IV slow push over 5-10 min. Can also be given as a continuous infusion.

Intranasal* and Nebulized Medications			
Generic	Dose	Max Dose	Comments
Fentanyl	IN: 1.5-2 mcg/kg q 1-2 h Neb: 1.5-4 mcg/kg	4 mcg/kg or 100 mcg	Divide dose equally between each nostril
Midazolam (5 mg/mL)	IN: 0.3 mg/kg	10 mg or 1 mL per nostril (total 2 mL)	Divide dose equally between each nostril
Lidocaine	Neb: 4% (40 mg/mL) 100-200 mg or 2.5-5 mL	4.5 mg/kg total or 300 mg	>5 mg/kg associated with serious toxicity

*Use MOST concentrated form available with atomizer. Limit 1 mL/nare. Ketamine: see separate Ketamine table.

Nerve Blocks

Type of Block	General Distributions of Anesthesia
Axillary Plexus Block	Forearm, wrist and hand. Elbow if including musculocutaneous nerve
Deep Peroneal Block	Web space between 1st and 2nd toes
Femoral Nerve Block	Anterior thigh, femur, knee and medial leg distal to the knee
Intraclavicular Plexus Block	Mid humerus, elbow, wrist and hand
Interscalene Plexus Block	Shoulder, upper arm, lateral 2/3 clavicle
Median Nerve Block	Anterior forearm, palm of hand (lateral portion) and digits 1-4 ½
Popliteal Nerve Block	Posterior lateral leg distal to knee, ankle and foot
Radial Nerve Block	Lateral arm, posterior forearm, dorsal hand, digits 1-4 ½
Saphenous Nerve Block	Distal medial thigh, medial knee, medial ankle and medial foot
Superficial Peroneal Block	Dorsal surface of foot
Supraduclavicular Plexus Block	Upper arm, elbow, wrist and hand
Sural Nerve Block	lateral ankle and foot
Tibial Block	Plantar surface of foot
Ulnar Nerve Block	Medial Forearm, medial hand and digits 4 ½ to 5

Local Anesthetic†	Onset	Duration without Epi (h)	Duration with Epi (h)	Max Dose without Epi, mg/kg	Max Dose with Epi, mg/kg
Bupivacaine (0.5%)*	Slow	2-4	4-8	2.5	3
2-Chloroprocaine (3%)	Rapid	0.5-1	—	10	—
Lidocaine (1%, 2%)	Rapid	0.5-2	1-6	4.5 (300 mg)	7 (500 mg)
Mepivacaine (1%, 2%)	Rapid	2-3	—	5	—
Ropivacaine (0.5%)	Medium	3	—	2-3	—

*†Most cardiotoxic: †0.5% = 5mg/mL, 1% = 10mg/mL, 2% = 20mg/mL

Skeletal Muscle Relaxants

Generic (Brand)	Starting Dose	Max Dose
Baclofen (Lioresal®)*	5 mg PO TID	80 mg/day
Cyclobenzaprine (Flexeril®)	5 mg PO TID	30 mg/day
Tizanidine (Zanaflex®)*	2-4 mg PO q 6-8 h prn	36 mg/day
Methocarbamol (Robaxin®)	1-1.5 g PO TID to 4x/day x 48-72 h, then 500-750 mg PO TID; 1 g V/IM q 8 h	8 g/day PO 3 g/day V/IM
Diazepam (Valium®) [CIV]	Adult: 2-5 mg PO q 6-8 h; 5-10 mg IV/IM Pediatric: (> 6 mo) 1 mg to 2.5 mg PO q 8 h prn; 0.04-0.2 mg/kg IV/IM q 2-4 h	Peds: 0.6 mg/kg/8h IV/IM to adult max
Orphenadrine (Norflex®)	100 mg PO BID, 60 mg IV/IM q 12 h	—

*Requires dose adjustment based on renal function.

Neuropathic Pain Medications

Generic (Brand)	Starting Dose	Max Dose
Gabapentin (Neurontin®)*	300 mg PO QHS to TID	3600 mg/day
Pregabalin (Lyrica®) [CV]†	50 mg PO TID	600 mg/day**
SNRI: Duloxetine (Cymbalta®)*	30 mg PO daily†	60 mg/day**
SNRI: Venlafaxine ER (Effexor XR®)*	37.5 mg PO daily	225 mg/day
TCA: Amitriptyline (Elavil®)	10-25 mg PO QHS	150 mg/day
Nortriptyline (Pamelor®)	10-25 mg PO QHS	150 mg/day

†See labeling recommendations for dose titration. †30 mg daily for at least 7 days to decrease nausea
**Varies depending on indication
*Requires dose adjustment based on renal function

Drug Interactions Important in Clinical Dentistry

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DENTAL DRUG	INTERACTING DRUG	RESULT/MANAGEMENT
ANTIBIOTICS		
<u>Penicillins</u>		
All Penicillins	Bacteriostatic antibiotics (clindamycin, erythromycin, tetracyclines)	Static agent may impair action of penicillins. Consult with other prescriber for modification.
Rare decrease in OC effectiveness with >48 hours of antibiotic therapy. Recommend additional barrier contraception for the remainder of the Pill package.	Methotrexate (Rheumatrex, g)	High dose penicillins may decrease 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.
<u>Cephalosporins</u>		
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.
<u>Lincomycins</u>		
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.
<u>Macrolides/Azalides</u>		
<u>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</u>	Alfentanil	Alfentanil actions increased. Use caution.
	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.

<p><u>Macrolides(excluding azithromycin)</u></p>	<p>Ergotamine Methylprednisolone</p> <p>Penicillins Pimozide (Orap)</p> <p>SSRIs (citalopram, escitalopram, fluoxetine, Sertraline, vilazodone)</p> <p>"Statins" (except fluva-, pitava-prava)</p> <p>Theophyllines</p> <p>Tolterodine (Detrol)</p>	<p>Acute ergotamine toxicity. Use cautiously Steroid clearance may be decreased. Caution.</p> <p>possible antagonism. Avoid static with cidal Avoid all macrolides-risk of sudden death</p> <p>AVOID CONCURRENT USE MACROLIDES DECREASE METABOLISM OF LISTED SSRIS.MONITOR..</p> <p>Increased statin levels with possible muscle toxicity. AVOID CONCURRENT USE</p> <p>Increased theophylline levels (20-25%). Decreased erythromycin levels may also occur. AVOID CONCURRENT USE if possible. SBE prophylaxis should not cause problems. Increased Detrol effects causing arrhythmias</p>
<p><u>Metronidazole</u> (Flagyl, Flagyl ER, Prostat, g)</p>	<p>Anticoagulants (Coumadin)</p> <p>Barbiturates Cholestyramine (Questran, g) Cimetidine (Tagamet, g)</p> <p>Disulfuram (Antabuse)</p> <p>Ethanol (IV diazepam, IV TMP-SMZ)</p> <p>Lithium</p> <p>Phenytoin (Dilantin) Quinidine Tacrolimus (Prograf)</p>	<p>Risk of bleeding disorders is increased in anticoagulated patients. Consult MD. Decreased metro. Levels. Increase dose. Reduced absorption of metronidazole Metronidazole levels may increase. Not sig.</p> <p>Concurrent use may result in acute psychosis or confusion. Risk of disulfuram-type reaction. AVOID CONCURRENT USE. Increased lithium levels with possible toxicity. Consult MD. Eff. of phenytoin may be incr. Monitor closely. Increased Quinidine levels. Monitor closely. Metronidazole doubles Prograf levels</p>
<p><u>Tetracyclines</u></p> <p>All Agents (doxycycline, minocycline, tetracycline)</p> <p>Doxycycline (Vibramycin, Periostat??)</p> <p>Tetracycline (Sumycin, Panmycin)</p> <p><u>Quinolones: all prolong QT interval</u> All Agents: Ciprofloxacin (Cipro,g) Levofloxacin (Levaquin) Moxifloxacin (Avelox) Ofloxacin (Floxin)</p> <p>Ciprofloxacin</p>	<p>Antacids containing Al, calcium, magnesium</p> <p>Bismuth (Pepto-Bismol)</p> <p>Iron Salts</p> <p>Oral Contraceptives</p> <p>Carbamazepine (Tegretol)</p> <p>Methotrexate (highdose IV)</p> <p>Phenobarbital</p> <p>Phenytoin (Dilantin, g)</p> <p>Colestipol (Colestid)</p> <p>Food (Milk and Dairy)</p> <p>Zinc sulfate</p> <p>Antacids (iron, sucralfate, zinc) Anticoagulants (Coumadin, g)</p> <p>Antineoplastics Cimetidine (Tagamet, g) Cyclosporine (Sandimmune, Neoral) NSAIDs Probenecid (Benemid, g) Theophylline Caffeine</p>	<p>Reduced serum concentrations of tets. Space administration by 1-2 hours.</p> <p>Inhibition of tetracycline absorption. Avoid concomitant administration.</p> <p>Decreased absorption of tets. Space use by 2-3h. Doxy always affected.</p> <p>Slightly increased risk of ovulation. Use additional method during cycle.</p> <p>Metabolism of doxy increased. Monitor response to doxycycline. AVOID DOXYCYCLINE WITH IV METHOTREXATE Decreased serum levels and effect of doxy. Monitor clinical response. Phenytoin stimulates doxy metabolism. Increase doxy dose or use other tet. Colestipol binds tet in intestine. Do not administer concomitantly. Decreased absorption of tet. Space use by 2-3 hours. Tetracycline absorption is decreased. Space use by 2-3 hours.</p> <p>Decreased quinolone absorption. AVOID CONCURRENT USE. Increased risk of bleeding disorders. Monitor INR. Quinolone serum levels may be decreased. Quinolone serum levels may be increased. Cyclosporine renal toxicity may be enhanced. Enhanced CNS stimulation Quinolone serum level may be increased 50%. Increased theophylline toxicity possible with Cipro and other. Consult MD Increased caffeine effects are possible.</p>

ANTIFUNGALS

Systemic Azole Agents (fluconazole, itraconazole, ketoconazole): all agents prolong QT interval

	Anticoagulants (Coumadin)	Increased risk of bleeding disorders in anticoagulated patient. Consult MD.
	Benzodiazepines	Alprazolam, triazolam are contraindicated with itraconazole and ketoconazole. AVOID
	Cyclosporine (Sandimmune, 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
fluconazole (Diflucan)	Zolpidem (Ambien)	Increased Ambien effect. Caution.
	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 <u>but</u> CCBs) (ACEI,B-blockers, diuretics)	Decreased antihypertensive effect. Monitor Blood Pressure.
	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

<u>Ibuprofen (Motrin, g)</u> <u>Ketorolac (Toradol,g)</u> <u>Sulindac</u>	Digoxin Salicylates DMSO	Possible increase in digoxin levels. Increased Ketorolac free drug conc. Decreased sulindac effectiveness and severe peripheral neuropathy. Avoid concurrent use.
<u>Sulindac</u> <u>Acetaminophen only</u>	Lithium Barbiturates, Carbamazepine, Phenytoin, Rifampin, Sulfipyrazone	Lithium levels remain constant or decrease. 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.
<u>Tramadol (Ultram, Ultracet, g)</u>	Any drug that enhances serotonin activity(SSRI antidepressants, "triptans" for acute migraine Carbamazepine (Tegretol,g) MAOI's () Quinidine	Possible serotonin syndrome. AVOID CONCURRENT USE. Decreased tramadol levels MAOI toxicity enhanced Tramadol increased/metabolite decreased
	Ritonavir (Norvir)	Increased Tramadol effect. AVOID COMBO.
NARCOTIC ANALGESICS		
<u>Opioid analgesics</u>	Alcohol, CNS depressants, local anesthetics, antidepressants, antipsychotics, antihistamines, cimetidine Antimuscarinics and antidiarrheals (e.g. atropine), antihypertensives (e.g. guanadrel) Buprenorphine, nalbuphine, naltrexone	Increased CNS and respiratory depression may occur. Use cautiously. Opioids increase the effects of these drugs. Use cautiously. These drugs block the analgesic effects of opioids. Substitute with NSAIDs.
<u>Codeine (Hydrocodone lesser extent)</u>	Lybalvi (olanzepine/samidorphan) 2D ₆ Inhibitors, Amiodarone, Cimetidine, Desipramine, Fluoxetine, Paroxetine, Propafenone, Quinidine, Ritonavir	Samidorphan is an opioid antagonist so d/c 7 days prior to use of opioid analgesic Inhibition of biotransformation of Codeine to active analgesic form. Use different narcotic on 2D ₆ Inhibitor patients.
<u>Meperidine (Demerol, g)/Fentanyl/All Fentanyl derivatives</u>	MAOIs (Marplan, Nardil, Parnate, Furoxone) selegiline (Eldepryl) Protease inhibitors Ritonavir (Norvir)	Hypertension/hyperpyrexia or coma and hypotension.AVOID CONCURRENT USE if MAOI taken within 14 days. Increased CNS/resp. depression- AVOID Large increase in meperidine. AVOID COMBO.
LOCAL ANESTHETICS		
<u>Amides</u> (e.g. lidocaine)	Alcohol,CNS depressants,opioids, antidepressants,antipsychotics, antihistamines Antiarrhythmic drugs Beta Blockers, cimetidine	Increased CNS and resp. depression may occur. Use caution. Increased cardiac depression. Metabolism of lidocaine is reduced. Use caution
<u>Esters</u> (e.g. procaine)	Anticholinesterases (Neostigmine) Sulfonamides	Metabolism of esters reduced. Inhibit sulfonamide action.
VASOCONSTRICTORS (epinephrine,levonordefrin)		
	Inhalation anesthetics (halothane) Tricyclic antidepressants-high dose (amitriptyline, desipramine, imipramine, nortriptyline, etc) Beta-blockers (nonselective) (e.g. propranolol, nadolol) Phenothiazines (e.g. chlorpromazine)	Increased chance of arrhythmia Increased sympathomimetic effects possible. Limit epi to 0.04mg with high dose TCA's. Hypertensive and/or cardiac rx possible. Limit epi to 0.04mg/2hr. visit. Vasoconstrictor action inhibited,leading to possible hypotensive responses. Use cautiously.
	Monoamine Oxidase Inhibitors (MAOIs) Selegiline (Eldepryl,g) COMT Inhibitors (Comtan, Tasmar)	Slight possibility of hypertensive rx. Slight possibility of hypertensive rx. Slight possibility of hypertensive rx.

AGENTS FOR PARENTERAL ANESTHESIA		
<u>Antihistamines</u>		
diphenhydramine (Benadryl) hydroxyzine (Atarax, Vistaril) Promethazine (Phenergan)	Anticholinergics CNS depressants (alcohol, narcotics)	Increased dry mouth, tachycardia, urinary retention. Monitor. Enhanced duration and intensity of sedation. Reduce dosages.
<u>Barbiturates</u>		
methohexital (Brevital,g)	CNS depressants (alcohol, narcotics) Furosemide (Lasix, g) Sulfisoxazole IV	Additive CNS and resp. depression Orthostatic hypotension Sulfa competes with barb. for binding sites. Smaller and more frequent barb. doses may have to be given.
<u>Benzodiazepines</u>		
diazepam (Valium,G)	CNS depressants (anticonvulsants, alcohol) Cimetidine,OCs,INH,Ketoconazole, Metoprolol, Omeprazole, Propoxyphene, Propranolol,Valproic Acid	Oversedation so may use slower titration. Decreased clearance of diazepam. Can avoid with lorazepam.
midazolam (Versed,g)	Digoxin Calcium Channel Blockers or CCBs (diltiazem-Cardizem, verapamil-Isoptin,Calan, Verelan) CNS depressants (alcohol, barbs) Erythromycin Narcotics (morphine, meperidine, fentanyl) Saquinavir (Fortovase) Thiopental	Increased digoxin levels. CCBs inhibit Cyp3A4 which prolongs the actions of midazolam. Evaluate patient factors to determine clinical significance. Increased risk of underventilation or apnea. May prolong the effect of midazolam. Increased midazolam levels. Monitor. Increased hypnotic effect of midazolam. More hypotension with Versed and Demerol. Increased midazolam levels. AVOID COMBO. After premed with Versed, decrease dose of thiopental for induction by 15%
<u>Narcotics</u>		
fentanyl (Sublimaze,g)	Barbiturate anesthetics Chlorpromazine (Thorazine, g) Cimetidine (Tagamet, g) Citalopram (Celexa,g) Diazepam Droperidol (Inapsine) MAOIs and furazolidone (Furoxone) Nitrous Oxide Ritonavir (Norvir)	Additive CNS and resp. depression. Increased toxicity of both agents. CNS toxicity case reports only. (confusion, apnea, Increased risk of serotonin syndrome With high dose fentanyl gives CV depression. Hypotension < pulmonary arterial pressure. Risk of hypertensive crisis.AVOID COMBO With high dose fentanyl may cause CV depress.
meperidine (Demerol, G)	Barbiturate anesthetics Chlorpromazine (Thorazine, g) Cimetidine (Tagamet, g) MAOIs and furazolidone (Furoxone) Phenytoin (Dilantin, g)	Increased fentanyl levels with Norvir Additive CNS and resp. depression Increased toxicity of both agents. CNS toxicity as with fentanyl. Meperidine has predictable and sometimes fatal reactions with use within 14 days. Type1 :coma,resp dep,cyanosis,low BP Type2:seizures,hyperpyrexia,hypertension,tac hy-cardia. AVOID CONCURRENT USE!!!! Decrease meperidine effects by increased hepatic metabolism
<u>Miscellaneous</u>		
etomidate (Amidate) ketamine (Ketalar,g)	Verapamil Barbiturates Thyroid Hormone Tubocurarine and nondepolarizing muscle relaxants CNS depressants (sedative/hypnotic, inhalation anesthetics, narcotics)	Possibility of prolonged anesthesia Prolonged recovery time. May produce hypertension/tachycardia Ketamine may increase neuromuscular effects and result in prolonged resp. depression. Increase CNS depression of propofol. Premed with narcotics may lead to more pronounced decrease in systolic, diastolic, and mean arterial pressures and cardiac output.
Propofol (Diprivan, G)		

