Oh the Pus! Oh the Pain!

Appropriate Antibiotic and Analgesic Prescribing

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Our Clinician:

Dr. Mark Donaldson BSP, RPH, PHARMD, FASHP, FACHE received his baccalaureate degree from the University of British Columbia and his Doctorate in Clinical Pharmacy from the University of Washington. He completed a residency at Vancouver General Hospital, and has practiced as a clinical pharmacy specialist, clinical coordinator and director of pharmacy services at many healthcare organizations in both Canada and the United States. He is currently the Associate Vice President of Clinical Pharmacy for Vizient’s Advisory Solutions, and lives in Whitefish, Montana.

Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon, and affiliate faculty in the School of Dentistry at UBC. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last 20 years focusing on dental pharmacology and dental therapeutics, and is a leader in the field.

Dr. Donaldson has published numerous peer-reviewed works and textbook chapters. He currently serves on the Editorial Board for the Journal Healthcare Executive and the Journal of the American Dental Association and is a reviewer for over ten other different journals. He is board certified in healthcare management and is the Past-President and current Regent of the American College of Healthcare Executives’ Montana Chapter. Dr. Donaldson was named as the 2014 recipient of the Bowl of Hygeia for the state of Montana and is the 2016 recipient of the Dr. Thaddeus V. Weclew Award. This award is conferred by the Academy of General Dentistry upon an individual who has made outstanding contributions to the medical, dental and pharmacy literature. Next week, Dr. Donaldson is to be conferred by the Canadian Dental Association (CDA) in Ottawa with the, “Special Friend of Canadian Dentistry Award for 2019.” This award is given to an individual outside of the dental profession in appreciation for exemplary support or service to Canadian dentistry and/or to the profession as a whole.

June 22, 2019
Bellevue, Washington
**Antibiotics and Dentistry**

**Sulphonamides**
- Sulphonamides first used in the 1930's.
- Penicillin first used in 1941, although Fleming had discovered it in 1929.
- Today we have more than 100 agents being used therapeutically.
- The development of newer antibiotics is in part due to the increased incidence of acquired bacterial resistance.

**Untoward Reactions to Sulphonamides**
- Disturbances of urinary tract.
- Disorders of hematopoietic system: acute hemolytic anemia, agranulocytosis, and aplastic anemia.
- Hypersensitivity reactions.
- Drug interactions: oral anticoagulants, sulfonylurea hypoglycemic agents, and hydantoin anticonvulsants.

**Classification of Penicillins**

<table>
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Example of Penicillin Resistant Mechanism
1. β-lactamases (penicillinases): inactivate penicillins by cleavage of the β-lactam ring.
2. Decreased affinity of PBPs for penicillin or decreased ability of penicillin to reach its site of action.

**β-lactamase Inhibitors**
Clavulanic acid: a product of *Streptomyces clavuligerus*, has poor intrinsic antimicrobial activity, but it is a “suicide” inhibitor (irreversible binder) of β-lactamases and inactivates them, thus preventing the destruction of β-lactam antibiotics.
- Augmentin: amoxicillin + clavulanic acid
- Timentin: ticarcillin + clavulanic acid

Resistant strains of bacteria are not necessarily more virulent than the susceptible strains of the same organism. Resistance makes these organisms more difficult to treat and limits our therapeutic options. One U.S. study estimated that the annual cost of antibiotic resistance was at least $100 million.

*2 million people in the U.S. are infected each year with antibiotic-resistant bacteria. This results in over 23,000 deaths and related healthcare costs of up to $20 billion.* Centers for Disease Control, 2015

*“Much of the resistance problem that we are facing today has been attributed to the overuse and misuse of antibiotics” (JAMA 1997;277:1794)*

**Other Notes or Questions to Ask:**
Therapeutic Uses in Dentistry

1. Treatment of an acute dental infection.
2. Prophylaxis in patients at risk of developing SBE or other problems as the result of bacteremia caused by dental procedures or traumatic injury.
3. Prophylaxis in patients with compromised host defense mechanisms caused by certain diseases or drug therapy.

The common infection, particularly those occurring as the result of carious lesions, are caused by a variety of aerobic gram-positive cocci and anaerobic microorganisms. Penicillin V has been historically the most frequently prescribed antibiotic for therapy of infections of dental origin. Some dental infections are caused by penicillinase-producing organisms: penicillinase-resistant penicillin or non-penicillin antibiotics such as erythromycin or clindamycin.

Oral Erythromycin and the Risk of Sudden Cardiac Death (NEJM 2004;351:1089-96): “The adjusted rate of sudden death from cardiac causes was twice as high as placebo and amoxicillin . . . The adjusted rate of sudden death from cardiac causes was 5 times as high among those who concurrently used CYP3A4 inhibitors.” “During 5 days of azithromycin therapy, there was a small absolute increase in cardiovascular deaths, which was most pronounced among patients with a high baseline risk of cardiovascular disease (NEJM 2012; 366:1881-1890).

Adverse Reactions of Penicillins
- Nausea, vomiting, and diarrhea.
- Penicillin G (in heroic doses): congestive heart failure (sodium cause), and cardiac toxicity (potassium cause, especially in patient with renal impairment).
- Neurotoxic effect (penicillin G in exceptionally high doses).
- Superinfections by nonsusceptible bacteria.

Acute allergic reactions (within 30 min): urticaria, angioedema, bronchoconstriction, gastrointestinal disturbances, and shock.
Accelerated allergic reactions (arise 30 min to 48 hrs): urticaria, pruritus, wheezing, mild laryngeal edema, and local inflammatory reactions.
Delayed allergic reactions (take 2 or more days to develop): skin rashes, may also be seen in oral cavity (acute glossitis, furred tongue, black and brown tongue, cheilosis, and severe stomatitis with loss of buccal mucosa).

The Bugs

Acute Dental Infections
- Tooth decay: Streptococcus mutans
- Pulpitis: Streptococci or Staphylococci
- Periapical Abscess: α-hemolytic Streptococci or Staphylococci
- Gingivitis: Peptococcus spp., Bacteroides

Prophylaxis for SBE (J Am Dent Assoc. 2007 Apr;138(4):458-74.)
Streptococcus viridans is the most common cause of infective endocarditis following dental procedures (more recently Staphylococcus epidermidis). Antibiotics are thought to provide protection by decreasing the number of organisms reaching the damaged heart valve from a primary source

Prophylaxis in the Immunocompromised
- Neutropenia Organ Transplantation
- HIV Infection Long-term immunosuppression (corticosteroid use)

Other Notes or Questions to Ask:
• How long of an antibiotic regimen is needed? Two common strategies:
  Patients complete all prescribed antibiotics, generally 5-10 days
  Patients stop taking antibiotics 48 hours after resolution of symptoms

• My patient forgot to premedicate. What do I do?
  According to the guidelines, the antibiotic should be given in a single dose 30 to 60 minutes
  before treatment. This time period is recommended so that there will be high blood levels of
  antibiotic at the time bacteremia occurs. The report adds that if the antibiotic inadvertently is not
  administered, the dosage may be given up to 2 hours after the procedure. However, it is important
  to note that the recommendation is to give the antibiotics 30 - 60 minutes before treatment.

If a patient is already receiving antibiotic therapy with a medication that is also recommended for
infective endocarditis (IE) prophylaxis, the guidelines state that it is prudent to select an
antibiotic from another class rather than to increase the dose of the currently administered
antibiotic. For example, if a patient is already taking amoxicillin, the dentist should select
clindamycin, azithromycin, or clarithromycin for IE prophylaxis.

Other Notes or Questions to Ask:
The Drugs:

- Penicillins
- Cephalosporins
- Sulphonamides
- Macrolides
- Fluoroquinolones
- Metronidazole
- Clindamycin

Concentration-dependant killing

Also known as dose-dependant killing, bacterial eradication is more rapid and efficient when the drug concentration is appreciably greater than the organisms MIC (e.g., Fluoroquinolones, Aminoglycosides).

Time-dependant killing

Also known as concentration-independent killing, bacterial eradication is best when the drug concentration remains constantly above the MIC (usually four times greater) during the dosing interval (e.g., β-lactams, vancomycin).

Bactericidal

- Penicillins
- Cephalosporins
- Imipenem
- Vancomycin
- Imipenem
- Aminoglycosides
- Metronidazole

Bacteriostatic

- Macrolides
- Tetracyclines
- Sulfonamides
- Clindamycin
- Trimethoprim
- (Chloramphenicol)

Other factors affecting a drug's efficacy:

- Diagnosis & initial antibiotic choice
- Route & time of administration
- Dose, frequency & duration of treatment
- Distribution of drug in the body
- Allergy status of the patient
- Side effects of the medication
- Patient compliance

AHA Guidelines: at-risk patients

**No penicillin allergy & able to take oral medication: Amoxicillin**

- Adult: 2g, 1h prior to procedure
- Child*: 50mg/kg 1h prior to procedure

**No penicillin allergy & unable to take oral medication: Ampicillin**

- Adult: 2g IM or IV, 30 min before procedure
- Child*: 50mg/kg IM or IV, 30 min before procedure

**Allergic to penicillin and able to take oral medication: Clindamycin**

- Adult: 600mg, 1h prior to procedure
- Child*: 20mg/kg, 1h prior to procedure
  - Or
  - Cephalexin† or Cefadroxil†
    - Adult: 2g, 1h prior to procedure
    - Child*: 50mg/kg, 1h prior to procedure
  - Or
  - Azithromycin or Clarithromycin
    - Adult: 500mg, 1h prior to procedure
    - Child*: 15mg/kg, 1h prior to procedure

Other Notes or Questions to Ask:
Allergic to penicillin and unable to take oral medication:

**Clindamycin**
- Adult: 600mg IV, within 30 min prior to procedure
- Child*: 20mg/kg IV, within 30 min prior to procedure

**Cefazolin**
- Adult: 1g IM or IV, within 30 min prior to procedure
- Child*: 25mg/kg IM or IV, within 30 min prior to procedure

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**Cardiac conditions associated with the highest risk of adverse outcome from endocarditis for which prophylaxis with dental procedures is recommended.**

- Prosthetic cardiac valve
- Previous infective endocarditis
- Congenital heart disease (CHD):
  - Unrepaired cyanotic CHD, including palliative shunts and conduits
  - Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six months after the procedure?
  - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
- Cardiac transplantation recipients who develop cardiac valvulopathy

*Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD.
† Prophylaxis is recommended because endothelialization of prosthetic material occurs within six months after the procedure.

“We found that although most patients reported receiving instructions for infectious endocarditis (IE) prophylaxis use consistent with American Heart Association guidelines, IE prophylaxis overuse among negligible-risk patients and underuse among moderate-risk patients was common. Continued physician and patient education may lead to improved adherence to the current American Heart Association recommendations.”

*JAMA. 2000;284:68-71*


**Other Notes or Questions to Ask:**
Antibiotic Prophylaxis (AP) Prior to Dental Procedures for Joint Replacement Patients

In 1988, a group of selected orthopaedic surgeons (AAOS), dentists and infectious diseases specialists (IDSA) held a workshop in Chicago, sponsored by the American Dental Association (ADA), to address the issue of Antibiotic Prophylaxis (AP) prior to dental procedures for their joint replacement. As a result of this meeting, a paper was published in 1990 stating that there was limited evidence to support AP but still recommended it until additional information became available. 


Later in 1990, the Council on Dental Therapeutics of the ADA published the results of the 1988 meeting stating that there was very limited data to support the continuation of the use of AP for dental patients with prosthetic joints. In 1997, after continued collaboration, the ADA and American Academy of Orthopaedic Surgeons (AAOS) published an advisory statement on the dental management of patients with prosthetic joints. This statement was slightly modified in 2003 and exists as our current guidelines.


According to these current guidelines, prophylaxis is not recommended for pins, plates, and screws, or for otherwise healthy patients with total joint replacements. Patients at “greater” risk could be considered for prophylaxis:

Prostheses were less than two years old or those with “high risk” conditions such as:

- Inflammatory arthropathies (rheumatoid arthritis, SLE)
- Drug- or radiation-induced immunosuppression
- Previous joint infection
- Malnourishment
- HIV infection
- Insulin-dependent diabetes
- Hemophilia
- Malignancy

Other Notes or Questions to Ask:
In February 2009, without any involvement with organized dentistry or non-orthopaedic physician specialties, the AAOS published an “Information Statement” entitled “Antibiotic Prophylaxis for Bacteremia in Patients with Joint Replacements”.¹

“...it was developed as an educational tool based on the opinions of the authors. Readers are encouraged to consider the information presented and reach their own conclusions”.


While the 2003 ADA/AOOS guidelines state:

“The risk/benefit and cost/effectiveness ratios fail to justify the administration of routine antibiotic prophylaxis.”

This new 2009 AAOS Information Statement suggested a very different position:

“Given the potential adverse outcomes and cost of treating an infected joint replacement, the AAOS recommends that clinicians consider antibiotic prophylaxis for all total joint replacement patients prior to any invasive procedure that may cause bacteremia.”

There is no clear explanation or scientific basis for this change in position and herein lies the current controversy: which paper is the most correct?

Other Notes or Questions to Ask:
If one were to follow the informational statement of the AAOS authors, the following four assumptions would need to be met to believe the actions are in the best interest of the patient . . .

1. Bacteremia from oral flora arising from dental procedures causes “late prosthetic joint infections” (infections occurring 3 months after joint replacement surgery).

Fact: Analysis of reported cases of LPJIs demonstrates that joint infections are rarely caused by bacterial species common to the mouth and there is no credible evidence to link LPJIs with dental procedures.1-4


2. There is a temporal relation between dental procedures and “late prosthetic joint infections” (infections occurring 3 months after joint replacement surgery).

Fact: evidence of a temporal relationship between dental procedures and the onset of LPJIs is circumstantial.1


3. Antibiotic Prophylaxis prevents bacteremia from dental procedures and subsequent “late prosthetic joint infections” (infections occurring 3 months after joint replacement surgery).

Fact: there are case reports of late prosthetic joint infections occurring after dental procedures despite Antibiotic Prophylaxis.1,2


4. One cannot compare “late prosthetic joint infections” and infective endocarditis because of differing anatomy, blood supply, microorganisms and mechanisms of infection.

Fact: Even if there are differences in the anatomy, microbiology and possible pathogenesis of LPJI and IE, they do have in common the underlying mechanism of putative hematogenous spread from the mouth.

Of greatest interest is that the 2007 AHA recommendations reduce by about 90% the number of cardiac patients recommended for AP by the 1997 AHA guidelines, in spite of the fact that as many as 50% of cases of IE are caused by oral bacterial species.

An analogy could be made to infections of cardiovascular implantable electronic devices (CIED) which, like LPJIs, are almost exclusively caused by Staphylococcal and other non-oral flora. A recent AHA Statement on CIED-related infections states that,
“the predominance of Staphylococci as pathogens ... rather than oral flora suggests that antibiotic prophylaxis for dental procedures is of little or no value...” and “... there is currently no scientific basis for the use of prophylactic antibiotics prior to routine invasive dental, gastrointestinal, or genitourinary procedures to prevent CIED infections” 1-5


Given the opinion nature of the 2009 Information Statement, the AAOM (American Academy of Oral Medicine) feels that it should not replace the 2003 Joint Consensus Statement prepared by the three relevant organizations, the ADA, the AAOS and the IDSA.

J Am Dent Assoc 2011;142;159-165

Continue to follow the 2003 guidelines and make sure to consider Patient Factors as described above as well as Procedure Factors and Drug Factors to ensure appropriate prescribing if antibiotics are indicated.


Other Notes or Questions to Ask:
The VERY Latest

- The current best evidence failed to demonstrate an association between dental procedures and prosthetic joint infection (PJI).
- In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection.


The VERY, VERY Latest

Dental Patients with Total Joint Replacement
- The CDA (and COA and AMMI) released a consensus statement this summer that said, among other things, that routine antibiotic prophylaxis is not indicated for dental patients with total joint replacements, nor for patients with orthopedic pins, plates and screws.
- We have received a handful of inquiries about this (and will be publishing a ‘practice tip’ about this soon)
- The consensus statement is here: https://www.cdaadc.ca/en/about/position_statements/jointreplacement

Other Notes or Questions to Ask:
Better Medicine, Better Dentistry: Appropriate Analgesic Prescribing

Classification of Pain: Most Americans experience three or four types of pain per year. There are over 50 million Americans partially or totally disable by pain with an annual cost to the system of $336 billion (American Academy of Pain Medicine 2015). The goals of therapy for pain are to decrease the intensity, increase physical activity, appropriate use of medications, regulation of sleep patterns and moods, as well as reestablishing work habits.

Acute pain has a treatment goal of a cure. Most of the symptoms associated with chronic pain are not present. Chronic pain often results in dependence and tolerance, psychological component is a major problem, a significant environmental change and family involvement and insomnia. The treatment goal for chronic pain is rehabilitation, not a cure.

Treatment may involve one or more of the following pain management options: Physical, Psychological or Pharmacological. Physical management involves exercise, cutaneous stimulation, repositioning and counterstimulation (acupuncture). Psychological management involves relaxation techniques, patient education support groups and meditation. Pharmacological management involves non-opioid analgesics, opioid analgesics and co-analgesic medications.

Dentists write approximately 20 million prescriptions for analgesics annually in U.S.. The major indication in dentistry is to manage postoperative pain, requiring a prescription of only a few days duration. Most often the challenge is to give high enough doses over a few short days to cover the inflammatory period, without putting the patient at risk of adverse sequelae. Although the cornerstone of these prescriptions focus on the non-opioid analgesics and opioid analgesics, it is important to remember that most pain of dental origin is due to the inflammatory process, which is why non-steroidal antiinflammatory drugs (NSAIDs) make the most sense for treatment. Opioid-based medications act centrally and do not have antiinflammatory properties.

The Drug Armamentarium: We will discuss pharmacological pain management by dividing the discussion into Peripheral Analgesics (non-opioid analgesics), Central Analgesics (opioid analgesics), Co-Analgesics and Local Anesthetics.

Analgesics used for Postoperative Dental Pain

- Acetaminophen - Tylenol
- Aspirin - Aspirin (various)
- Ibuprofen - Advil, Motrin, Nuprin
- Flurbiprofen - Ansaid
- Diflunisal - Dolobid
- Naproxen - Naprosyn, Aleve
- Ketorolac - Toradol
- Ketoprofen - Orudis
- Etodolac – Lodine
- Codeine - Codeine (in various)
- Oxycodone - Percocet, Percutan
- Meperidine - Demerol
- Pentazocine - Talwin
- Hydrocodone - Lortab, Vicodin
- Dihydrocodeine - Synalgos-DC
- Propoxyphene - Darvon

* Propoxyphene-containing products such as Darvon were removed from the US market in 2010.

Other Notes or Questions to Ask:
Peripheral Analgesics: non-Opioid Analgesics

**Acetaminophen** may be the most ubiquitous medication in this category. It is comparable to ASA and NSAIDs in analgesic and antipyretic activity, but only has a weak anti-inflammatory activity. In patients who are maintained on blood thinners or have a history of bleeding complications, acetaminophen dose offer one major advantage over ASA and NSAIDs as it has a minimal antiplatelet effect and does not injure the gastric mucosa. Adult dosages range from 325mg to 1000mg administered three to four times per day, with a maximum daily dose of no more than 4.0 grams (4000mg) to avoid hepatotoxicity. In those patients at risk for liver problems (e.g., Chronic alcoholics, hepatitis patients), the maximum recommended dose should not exceed 2.0 grams (2000mg). The pediatric dose of acetaminophen is 10-15 mg/kg/dose orally every 4-6 hrs (maximum 5 doses/day).

**Prostaglandins** generated during tissue damage direct some actions of inflammation: fever, pain and vasodilation. Inhibiting prostaglandin synthesis leads to a decrease in this response, which led to the advent of **NSAIDs** as an alternative to acetaminophen.

The mechanism of action of NSAIDs is to block the conversion of arachidonic acid to prostaglandins. Arachidonic acid is a by-product of the breakdown of injured cell membrane phospholipids by the enzyme phospholipase. Non-selective **COX inhibitors** not only block the inflammatory prostanoids which produce pain, tenderness, vasodilation and fever, but they also inhibit the cytoprotective prostanoids that maintain a normal gastric mucosa and normal platelet aggregation. **COX-2 inhibitors** only block the inflammatory prostanoids and do not effect the protective gastric mucosa and hemostasis.

There are a plethora of NSAIDs on the market and rather than reviewing each one individually, some key points should be stressed. Be familiar with at least three agents and their usual dosing regimens and maximum daily dosages. Some examples are:

- Ibuprofen (Motrin) 400-600 mg four times a day (max daily dose is 2400mg)
- Diclofenac (Voltaren) 25-50mg two or three times a day (max daily dose is 200mg)
- Naproxen (Naprosyn) 250-500mg two or three times a day (max daily dose is 1500mg)


**Other Notes or Questions to Ask:**
**NSAID Mortality:** Fortunately or unfortunately, many of these medications are now available without a prescription, which may give prescribers the false sense that they are completely “safe” (without adverse sequelae). In fact, **16,500 people die in US each year due to NSAID complications.** The mechanism of action of NSAID’s is to inhibit both COX-1 and COX-2 (cyclooxygenase isoenzymes) which are responsible for the production of prostaglandins: the mediators of inflammation. Some of these prostaglandins are cytoprotective, however, as part of the body’s natural homeostatic process. By nonspecifically inhibiting both isoenzymes, NSAIDs have been associated with an increased rate of gastritis, gastric erosion and even ulceration.


**Baseline Risk of Peptic Ulceration:** Hospitalization risk due to peptic ulceration is about 0.2% per year in non-NSAID users. The risk increase to 0.8% in patients currently taking NSAIDs and GI hemorrhage is the most common presentation. The risk is higher in men than women. The range of risk is from 0.5% to 1.7% depending on dose, drug and duration.

**NSAID Prescribing:** Not all NSAIDs are created equally. The risk of GI toxicity varies from: **ibuprofen → ASA → diclofenac → naproxen → indomethacin → piroxicam → ketoprofen → ketorolac.** When you prescribe NSAIDs, do so only to patients who do not respond to acetaminophen. Select the NSAID with the lowest toxicity and prescribe the lowest possible dose for the shortest duration of time. The use of NSAIDs may be considered relatively safe when prescribed at the most effective dose and for the shortest duration of time, which was defined as 10 days or fewer.


**COX - 2 INHIBITORS:**

COX-2 Inhibitors were developed to decrease GI effects of NSAIDS. Older NSAID’s inhibit both COX-1 and COX-2 prostanoids. COX-1 is responsible for protecting the GI mucosa (cytoprotective). COX-2 is responsible for inflammatory mediation. COX-2 selectivity increases from:

**ketorolac → ketoprofen → indomethacin → ASA → ibuprofen → piroxicam → diclofenac → celecoxib → meloxicam**

**Other Notes or Questions to Ask:**
When rofecoxib (Vioxx) was available, it was the most selective of available NSAIDs (>50-fold potency for COX-2 over COX-1) and was is twice as selective as celecoxib. Vioxx was unfortunately removed from the US market in 2004. The COX-2 inhibitor seem to be equally effective as the NSAIDs. There seems to be no difference in overall adverse effects. There seems to be no difference in real effects. In these 3 studies no dyspeptic symptom differences were noted. However, there was an absolute difference in endoscopically proven ulcer of 10 – 25% decrease. Also note that where COX-2 inhibitors were used, they had no effect on platelets.

**Differences between the COX-2s:** If a patient has a sulfa allergy you should avoid the Celecoxib/Valdecoxib medications. There still is a question if one should not prescribe COX-2s if an aspirin allergy exists. Recognize that Celecoxib has a slightly slower onset of activity. Obviously, with the removal of **Vioxx** & **Bextra** from the market, adverse effects can not be ruled out!

**When to use a COX-2?** Use a COX-2 inhibitor if other less expensive NSAIDs have been shown to be ineffective or not tolerated. Use a COX-2 inhibitor if cost is not an issue. Use a COX-2 inhibitor if your patient is controlled on a blood thinner like coumadin. Use a COX-2 inhibitor if you are planning to use misoprostol with an NSAIDS.

These newer medications can be up to ten times more expense than the traditional NSAIDs, and should generally be reserved for those patients who have failed prior treatment with NSAIDs, or if they are controlled on a blood thinner like coumadin.

- **rofecoxib (Vioxx)** 50mg QD
- **veldecoxib (Bextra)** 10mg QD
- **celecoxib (Celebrex)** 200mg BID


**What about the use of Steroids?**

Dexamethasone is a glucocorticoid (FDA approved 1958). Supplied as Tablets (0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg); Injection (4mg/mL, 10mg/mL, 20mg/mL); Elixir (0.5 mg/5 mL)

Plasma Half-Life: 3-5 hours  
Duration of Action: 2.5-6 days to treat pain, swelling and trismus.


**Other Notes or Questions to Ask:**
Opioid-Based Analgesics: Central Analgesics

When to use them: Opioids such as morphine, meperidine, hydromorphone, fentanyl and others should not always be considered the drugs of choice for all postoperative analgesia cases. They act centrally, have no effect on the inflammatory process, and are associated with adverse sequelae in many patients ranging from constipation to more acute narcotizing effects.

How to use them: Having said this, they may still have a role in pain management, as interpatient response to any type of drug therapy is highly variable. The same general prescribing guidelines described above hold true for opioid-based analgesics: be familiar with at least three agents and their usual dosing regimens. Be aware of drug interactions with other CNS depressant. Most drug interaction software available today does not recognize the obvious interactions between opioid and benzodiazepines.

Pain Control: the site of action for the opioid narcotics is in the brain stem. Where as NSAIDs and COX-2 inhibitors work at the site of injury.

Maximum daily dosages do not readily apply to these agents and it may be more clinically useful to be aware of the minimum effective dosages and potential equiefficacious dosing when switching between agents.

In trying to achieve the best of both worlds there are several combination products which incorporate either acetaminophen or an NSAID with an opioid-based analgesic (eg. Percocet, Vicodin, and Vicoprofen). The practitioner should still decide if an opioid-based analgesic is appropriate therapy for the particular case, and they should also be aware of the maximum recommended daily doses of acetaminophen or the NSAID being used in the combination product. This is especially important in those patients who are ordered both Tylenol and Percocet, for example (since they both contain acetaminophen).

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</tbody>
</table>

Equianalgesic dosing tables are available for opioid-based analgesic medications, which aid in prescribing or changing a patient’s regimen to a different agent, but it must be stressed that these are only guidelines and are usually based on single-dose studies in healthy individuals. Some examples of these guidelines are shown below:

Other Notes or Questions to Ask:
1 x Tylenol #3 = 300mg Acetaminophen + 30mg Codeine 
2 x Tylenol #3 = 10mg oral Morphine 
1 x Vicodin = 500mg Acetaminophen + 5mg Hydrocodone 
2 x Vicodin = 10mg oral Morphine 
1 x Tylenol #3 = 1 x Vicodin tablet

**Morphine:** Morphine is still the gold standard in pain control because of the wide rage of dosage forms and low cost. There are even sustained release preparations that allow a dose once every 12 hours. These sustained release medications are MS Contin, M-Eslon, Kadian. In the elderly M=Eslon offers some advantages because the capsule can be pulled apart and contents mixed as long as the granules are not crushed.

**Hydromorphone (Dilaudid):** This drug is excellent for patients allergic to morphine. Dilaudid SR (sustained release) comes in 3, 6 and 12mg capsules. The dosing is every 12 hours and the capsules can be opened. This drug is also effective when morphine tolerance develops. You should switch from morphine to hydromorphone when morphine doses needed by the patient are increasing rapidly. In the non-narcotic naïve patient the ratio is about 5:1.

**Meperidine (Demerol):** There is no advantage with Demerol over morphine for chronic pain. This drug has a shorter half-life, but its active metabolite (normeperidine) has an extended half-life of 8-12 hours. Meperidine may accumulate with repeated administration leading to CNS stimulation that manifests itself as agitation, irritability, nervousness, tremors, twitching and seizures. Since this drug is eliminated by the kidneys, patients with decreased renal function are more susceptible to CNS stimulation from repeated administration. A major contraindication is in patient receiving MAO inhibitors. This may cause severe respiratory depression, coma and decrease in blood pressure.

**Fentanyl (Duragesic):** Fentanyl can be useful if enteral narcotics are not an option. The dose is limited to 25, 50 75 and 100mcg increments. One need to wait 24 hours to evaluate the effectiveness for pain control. This drug is not for acute pain! It may take 6 days after increasing the dose before a new steady state level is achieved. If the drug is administered in a patch, the serum concentration will take approximately 17 hours to re-equilibrate.

**Other Opioids:** Codeine is a relatively weak analgesic. Oxycodone and Hydrocodone usually are in combination products such as Percocet and Vicodin. Be aware that because of these combination products a toxicity level may be reached if doses of acetaminophen exceed 4 grams per day.

**Constipation:** ... the eleventh commandment? “the hand that writes the narcotic order shall write the laxative order!”

**Other medications for pain: TCA Antidepressants** such as amitriptyline, nortriptyline and imipramine are examples. SSRI (Selective Serotonin Reuptake Inhibitors) Antidepressants such as fluoxetine (Prozac), sertraline (Zoloft), citalopram (Celexa) and escitalopram (Lexapro) are examples. Anticonvulsants such as valproate (Epival), carbamazepine (Tegretol) and gabapentin (Neurontin) are examples. Finally Glucocorticoids such as dexamethasone, prednisone, methylprednisolone and hydrocortisone are examples.

**Efficacy of Tramadol:** Ibuprofen>Tramadol/Acetaminophen>acetaminophen>Tramadol>Placebo

**The VERY Latest:** “If dentists do prescribe opioid containing analgesics, it is important to consider limiting these prescriptions to 12 doses or fewer, because larger quantities often result in leftover medication that can be at risk for diversion.”


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**Other Notes or Questions to Ask:**