Appropriate Analgesic Prescribing

Mark Donaldson, BSP, PHARMD, ACPR, FASHP, FACHE

Our Clinician:

Dr. Mark Donaldson received his baccalaureate degree from the University of British Columbia, and his Doctorate in Clinical Pharmacy from the University of Washington. He has further completed a residency at Canada's largest tertiary care facility, Vancouver General Hospital, and is the current AVP of Clinical Pharmacy Performance Services for Vizient, living in Whitefish, Montana. Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, and Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last seventeen years focusing on dental pharmacology and the art of dental therapeutics, and has become a leader in this field of study. Dr. Donaldson has a number of published works in the peer-reviewed literature and spent three years in Japan focusing on cross-cultural communication and internationalization. He currently serves on the Editorial Board for the Journal of the American Dental Association. He is board certified in healthcare management and is the current President of the American College of Healthcare Executives’ Montana Chapter. Dr. Donaldson is the 2016 recipient of the AGD’s Dr. Thaddeus W. Weclew Award.
“The dentist retains the primary responsibility for the procedures actually carried out and for the immediate management of any untoward complications.”

READ YOUR REGULATIONS
(Effective 1/26/19)


**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 $356 billion (American Academy of Pain Medicine 2017). 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.

Other Notes or Questions to Ask:
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.

<table>
<thead>
<tr>
<th>Analgesics used for Postoperative Dental Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen - Tylenol</td>
</tr>
<tr>
<td>Aspirin - Aspirin (various)</td>
</tr>
<tr>
<td>Ibuprofen - Advil, Motrin, Nuprin</td>
</tr>
<tr>
<td>Flurbiprofen - Ansaid</td>
</tr>
<tr>
<td>Diflunisal - Dolobid</td>
</tr>
<tr>
<td>Naproxen - Naprosyn, Aleve</td>
</tr>
<tr>
<td>Ketorolac - Toradol</td>
</tr>
<tr>
<td>Ketoprofen - Orudis</td>
</tr>
<tr>
<td>Etodolac – Lodine</td>
</tr>
<tr>
<td>Codeine - Codeine (in various)</td>
</tr>
<tr>
<td>Oxycodone - Percocet, Percodan</td>
</tr>
<tr>
<td>Meperidine - Demerol</td>
</tr>
<tr>
<td>Pentazocine - Talwin</td>
</tr>
<tr>
<td>Hydrocodone - Lortab, Vicodin</td>
</tr>
<tr>
<td>Dihydrocodeine - Synalgos-DC</td>
</tr>
<tr>
<td>Propoxyphene - Darvon</td>
</tr>
</tbody>
</table>

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

WAC 246-817-913
Treatment plan—Acute nonoperative pain and acute perioperative pain.
(1) The dentist shall consider prescribing nonopioid analgesics as the first line of pain control in patients in accordance with the provisions of WAC 246-817-908 unless not clinically appropriate.

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)

**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
- valdecoxib (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.

WAC 246-817-911: Diagnosis identified on prescription. The practitioner shall include the diagnosis, indication for use, or the International Classification of Diseases (ICD) code on all opioid prescriptions (effective 1/26/19).

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 (e.g., 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).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Equianalgesic dose</th>
<th>Duration of Action (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>IM, SC PO</td>
<td>10mg</td>
<td>4-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30-60mg</td>
<td>4-6</td>
</tr>
<tr>
<td>Meperidine</td>
<td>IM, SC PO</td>
<td>100mg</td>
<td>2-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200mg</td>
<td>2-4</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>IM, SC PO</td>
<td>2mg</td>
<td>4-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-8mg</td>
<td>4-5</td>
</tr>
<tr>
<td>Oxycodone/</td>
<td>PO</td>
<td>30mg</td>
<td>3-4</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>IM, PO</td>
<td>60mg</td>
<td>4-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120-180mg</td>
<td>4-6</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>IM Transderm</td>
<td>0.1-0.2mg</td>
<td>Very short</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25µg/hr</td>
<td>72</td>
</tr>
</tbody>
</table>

Other Notes or Questions to Ask:
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:

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 x Tylenol #3</td>
<td>300mg Acetaminophen + 30mg Codeine</td>
</tr>
<tr>
<td>2 x Tylenol #3</td>
<td>10mg oral Morphine</td>
</tr>
<tr>
<td>1 x Vicodin</td>
<td>500mg Acetaminophen + 5mg Hydrocodone</td>
</tr>
<tr>
<td>2 x Vicodin</td>
<td>10mg oral Morphine</td>
</tr>
<tr>
<td>1 x Tylenol #3</td>
<td>1 x Vicodin tablet</td>
</tr>
</tbody>
</table>

**Morphine:** Morphine is still the gold standard in pain control because of the wide range 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 Notes or Questions to Ask:
WAC 246-817-916 Treatment plan—Subacute pain.

(3) If the dentist prescribes opioids for effective pain control, such prescriptions must not be in a greater quantity than needed for the expected duration of pain severe enough to require opioids (fourteen-day supply).

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 (Epilevel), 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

WAC 246-817-915

**Patient evaluation and patient record.**

(d) Conduct, or cause their designee to conduct, a query of the PMP in accordance with the provisions of WAC 246-817-980 to identify any Schedule II-V medications or drugs of concern received by the patient and document in their review and any concerns.


One in 16 patients prescribed opioids after a surgical procedure will become a long-term user.


An estimated 70,000 people died in the United States due to an opioid-related drug overdose in 2017.


Other Notes or Questions to Ask:

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Saturday, April 20, 2019

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WAC 246-817-980
Prescription monitoring program - Required registration, queries, and documentation.
(1) The dentist shall register to access the PMP;
(2) At a minimum, the dentist shall ensure a PMP query is performed prior to the prescription of an opioid.


WAC 246-817-977
Coprescribing of naloxone.
The dentist shall confirm or provide a current prescription for naloxone or refer the patient to a pharmacist for further counseling and evaluation when opioids are prescribed to a high-risk patient.

**Naloxone (Narcan®) – Narcotic Antagonist**

**Indications:**
- Reversal of narcotic depression including respiratory depression induced by opioids, (both natural and synthetic narcotics), propoxyphene, and narcotic-antagonist analgesics
- Diagnosis of suspected acute narcotic overdosage
- Not effective in counter-acting depression due to barbiturates, tranquilizers or other non-narcotic anesthetics or sedatives

**Routes of Administration:**
- IM, SC - when IV route not feasible; onset of action not as prompt as with IV and may be delayed in patients who are hypotensive and have impaired peripheral circulation
- IV direct - slowly over at least 1 minute


**Dosage, Adults:**
- Known or suspected overdose: 0.4-2 mg IV; if no response, repeat 2-4 mg in minutes; in cases of large narcotic overdoses, or methadone, pentazocine, propoxyphene overdose, higher doses may be required; if no response after 10 mg, reassess diagnosis; effective dose may be repeated every 20-60 minutes
- Post-operative respiratory depression: 0.1-0.2 mg at 2-3 minute intervals until desired response is obtained; repeat doses may be required at 1-2 hour intervals

**Other Notes or Questions to Ask:**
• Partial reversal of opioid-associated respiratory depression in palliative patient: if respiratory rate < 6/minute, administer 0.1-0.2mg IV q2-3 minutes or 0.1-0.2mg SC q5-10minutes until respiratory rate > 10/minute. Continue to monitor respiratory rate q15minutes until no naloxone given x 1 hour.

Dosage, Children:
• Known or suspected overdose:
• Birth to 5 yrs or 20 kg: 0.1 mg/kg/dose; repeat at 2-3 minute intervals until desired response obtained
• > 5 yrs or > 20 kg: 2 mg; repeat as above
• Post-operative respiratory depression: 0.005-0.01 mg/kg IV repeated if necessary at 2-3 minutes intervals
• Onset of effect: within 1-2 minutes following IV, within 2-5 minutes following IM or SC
• Duration of effect: 45 minutes to 3-4 hours
• Since duration of action of narcotic agent may exceed that of naloxone, repeated doses or administration of naloxone via IV infusion may be required


**Medical Cannabinoids: “Going to Pot?”**

<table>
<thead>
<tr>
<th>Therapeutic Index (LD&lt;sub&gt;50&lt;/sub&gt; / ED&lt;sub&gt;50&lt;/sub&gt;)</th>
<th>Aspirin Therapeutic Index 23:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Graph](Pallasch, Anes Prog. 35:87-101,1988)</td>
<td>![Graph](Pallasch, Anes Prog. 35:87-101,1988)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Morphine Therapeutic Index 50:1</th>
<th>Marijuana TI is 40,000:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Graph](Pallasch, Anes Prog. 35:87-101,1988)</td>
<td>![Graph](Pallasch, Anes Prog. 35:87-101,1988)</td>
</tr>
</tbody>
</table>
The Case for Medical Marijuana

Lethal Smoked Dose: “1500 pounds smoked within 15 minutes” Annas GJ. NEJM 1997;337:435-9

GW Pharmaceuticals (www.gwpharm.com)
- Sub-Lingual Spray (53 Patients Multiple Sclerosis or Spinal cord Injury)
- Findings from phase I & II: 41 out of the first 53 derived statistically significant benefit, including reduced pain, improved sleep and overall symptom relief.
- Side effects, including headaches and nausea. Generally the ability to control dosage with the spray mechanism allowed users to strike a balance between reducing pain and getting high.

Johns Hopkins University
- Long-Term Pot-Use Study (N=1318)
- Effects of marijuana on cognition in persons under 65 followed for 15 years: No ill health effects filed and no significant differences in cognitive decline between, heavy-users, light-users and non-users of cannabis

Uses for Medical Marijuana

<table>
<thead>
<tr>
<th>Folklore</th>
<th>California &amp; Other States</th>
</tr>
</thead>
<tbody>
<tr>
<td>appetite</td>
<td>cancer</td>
</tr>
<tr>
<td>pain</td>
<td>anorexia (appetite)</td>
</tr>
<tr>
<td>seizures</td>
<td>AIDS</td>
</tr>
<tr>
<td>insomnia</td>
<td>chronic pain</td>
</tr>
<tr>
<td>spasticity</td>
<td>spasticity</td>
</tr>
<tr>
<td>depression</td>
<td>glaucoma</td>
</tr>
<tr>
<td>rheumatism</td>
<td>arthritis</td>
</tr>
<tr>
<td>migraine</td>
<td>migraine</td>
</tr>
<tr>
<td>menstrual cramps</td>
<td>hospice admission</td>
</tr>
<tr>
<td>PMS</td>
<td>any other illness ...</td>
</tr>
<tr>
<td>constipation</td>
<td></td>
</tr>
</tbody>
</table>

Cannabinoids

- marijuana contains over 400 chemicals (hundreds more produced when smoked)
- over 60 are cannabinoids: delta-9-tetrahydrocannabinol (THC) is the most psychoactive and is often used as a marker
- interacts with a cannabinoid system of receptors to produce an effect
- CB1 receptors are found in the central nervous system. First cloned in 1990 (concentrated in areas within the “reward system” of the brain); the action in the hippocampus may explain its ability to interfere with memory; the action in the cerebellum may be responsible for its ability to cause incoordination and loss of balance. CB1 also seems to be important in mediating pain relief, body temperature and gut activity
- CB2 receptors are found in the periphery. First cloned in 1993, they shares only 44% identity with CB1. They are present in lymphocytes and the monocyte/macrophage population of the spleen but not the brain (ie appear to be confined to the immune system). They may mediate the chemical communications between different types of immune cells or between sensory fibers and blood cells

Other Notes or Questions to Ask:
Oral Route
- Low bioavailability
- Slow onset
- First-pass metabolism to 11-OH-Δ9-THC which has three times the potency of THC and therefore increases psychoactive effects

Smoked
- Heat activated
- High bioavailability
- Rapid onset
- Bypasses gut for nausea
- Bypasses hepatic first-pass metabolism
- Long-term risks unknown

Can also be given via inhalation, sublingual, and rectal routes. There are respiratory risks when administering the drug via the smoked route which is why, as health care providers we cannot condone this delivery method: tar content may be greater than tobacco; irritates, increases airway resistance; lung damage with long-term use; long-term lung cancer risk unknown and; may be additive to tobacco-related risk. Water-pipes and vaporizers may improve the safety of the smoked route, however. Due to the high prevalence rate there has been more than just a suggestion made for the need for accurate screening pre-operatively or this risk factor may be missed. The possibility of cannabis withdrawal syndrome may be underestimated, and the patients should be observed for respiratory problems (as per tobacco).

Sativex® (approved 09/2005)
- Delta-9-tetrahydrocannabinol & cannabidiol
- For the symptomatic relief of neuropathic pain in adults with Multiple Sclerosis
- Peppermint flavoured buccal spray (2.7mg THC & 2.5mg CBD per spray)
- Initial dose: 1 spray sublingually q4h as needed
- Only in Canada at this time (Bayer Inc.)

Other Notes or Questions to Ask:
Old to New... Lidocaine to Exparel (liposomal bupivacaine)

- Based on a proprietary extended-release drug delivery technology called DepoFoam
- DepoFoam encapsulates drugs without altering their molecular structures and then releases them over a period of time
- Membrane components based on natural and well-tolerated sources

**Good news:**
- Up to 96 hrs of pain relief
- Can be injected at the time of surgery potentially decreasing the need for opioid analgesics

**Bad news:**
- Expensive
  - AWP of 20mL vial is $378 vs $50 for a box of bupivacaine dental
- Not approved for block anesthesia
- Cannot use other locals around the time of Exparel

Learn more at: www.Exparel.com

Other Notes or Questions to Ask: