Outpatient Pain Management Updates and Guidelines

Spring COP CE Program 2019
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In support of improving patient care, Idaho State University Kasiska Division of Health Sciences is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.
Disclosures

• The planners and presenter of this presentation have disclosed no conflict of interest, including no relevant financial relationships with any commercial interests
Objectives

• Discuss the mechanisms and benefits of adjunctive and off-label medications for pain management

• Incorporate evidence-based pain management guideline recommendations into individual patient care plans

• Educate patients and prescribers regarding methods shown to appropriately provide individual patients adequate pain management
The International Association for the Study of Pain

Definition:

PAIN is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".
As Learning- It is nice to categorize patients pain

- **Acute Pain:**
  - Tissue damage pain
    - Strain sprains
    - Overuse syndromes
    - Cuts
    - Surgery
  - Confined tissue damage pain
    - Malignancy
    - Bone pain
    - Dental pain
    - Fascial sheath pain
  - Headaches
    - Multiple covered elsewhere
  - Visceral vs cutaneous

- **Chronic Pain**
  - Malignant pain
    - Spreads other organs
  - Nerve pain
    - Parasthesias
    - Neuropathic pain
    - Post herpetic neuralgia (PHN)
    - Phantom limb
    - Wind up
  - Non-malignant chronic pain
  - Complex Regional Pain Syndrome
Nociception:
An unpleasant sensation occurring in varying degrees of severity as a consequence of injury, disease, or emotional disorder.
How Do you Quantitate Pain?

• Visual Analog Scales
  – What is the most accurate?

• Functionality:

• Improvement in Quality of Life
Measures of Analgesia

0-10 Numeric Pain Intensity Scale

0-10 Numeric Pain Distress Scale
Western Ontario McMasters Osteoarthritis (WOMAC)

- 24 items divided into 3 subscales:
  - Likert 0-4 or Visual analog 0-100
  - **Pain (5 items):** during walking, using stairs, in bed, sitting or lying, and standing
  - **Stiffness (2 items):** after first waking and later in the day
  - **Physical Function (17 items):** stair use, rising from sitting, standing, bending, walking, getting in / out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in / out of bath, sitting, getting on / off toilet, heavy household duties, light household duties
Measures of Anaglesic Efficacy
Comparative Drug Studies

• Pain Intensity Reduction
  – Total Pain Reduction 4, 8 hours (TOPAR)
  – Sum of Pain Intensity Differences (SPIRD)
  – Peak Pain Intensity Differences (PPIID)

• Functionality

• Other medication sparing effects
Table 2. Efficacy End Point Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>25 mg n = 49</th>
<th>50 mg n = 50</th>
<th>75 mg n = 50</th>
<th>100 mg n = 48</th>
<th>200 mg n = 50</th>
<th>Morphine sulfate 60 mg n = 51</th>
<th>Ibuprofen 400 mg n = 51</th>
<th>Placebo n = 51</th>
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</thead>
<tbody>
<tr>
<td>TOTPAR-8</td>
<td>6.3 (8.4)</td>
<td>7.9 (8.1)*</td>
<td>9.7 (8.5)*†</td>
<td>11.6 (8.2)*‡</td>
<td>15.3 (7.5)*§</td>
<td>13.8 (10.3)*§§</td>
<td>17.9 (9.9)*§§</td>
<td>4.7 (7.3)</td>
</tr>
<tr>
<td>TOTPAR-4</td>
<td>2.6 (3.5)</td>
<td>3.7 (3.6)</td>
<td>4.3 (3.7)</td>
<td>5.2 (3.7)↓</td>
<td>7.1 (3.5)♦</td>
<td>5.8 (4.6)↓</td>
<td>8.2 (4.6)↓</td>
<td>2.0 (2.9)</td>
</tr>
<tr>
<td>SPID-4</td>
<td>0.6 (2.3)</td>
<td>1.2 (2.9)</td>
<td>1.4 (2.9)</td>
<td>2.0 (3.0)↓</td>
<td>3.5 (2.7)↓</td>
<td>3.0 (3.4)</td>
<td>4.1 (3.6)</td>
<td>0.5 (2.5)</td>
</tr>
<tr>
<td>SPID-8</td>
<td>1.6 (5.3)</td>
<td>2.7 (6.5)</td>
<td>3.0 (6.4)</td>
<td>4.4 (6.6)↓</td>
<td>7.1 (6.0)↓</td>
<td>7.3 (7.7)↓</td>
<td>8.5 (7.3)</td>
<td>1.2 (5.9)</td>
</tr>
<tr>
<td>SPRID-4</td>
<td>3.3 (5.4)</td>
<td>4.9 (6.2)</td>
<td>5.7 (6.2)↓</td>
<td>7.2 (6.4)↓</td>
<td>10.6 (5.7)</td>
<td>8.9 (7.8)↓</td>
<td>12.3 (7.8)</td>
<td>2.5 (5.1)</td>
</tr>
<tr>
<td>SPRID-8</td>
<td>7.9 (13.0)</td>
<td>10.6 (13.8)</td>
<td>12.6 (14.3)</td>
<td>15.9 (4.2)↑</td>
<td>22.5 (12.7)↑</td>
<td>21.1 (17.6)†</td>
<td>26.2 (16.5)†</td>
<td>5.9 (12.5)</td>
</tr>
<tr>
<td>PPR</td>
<td>1.2 (1.4)</td>
<td>1.5 (1.4)</td>
<td>1.7 (1.3)</td>
<td>2.2 (1.3)↑</td>
<td>2.8 (1.0)↑</td>
<td>2.3 (1.6)</td>
<td>2.8 (1.5)↑</td>
<td>0.9 (1.2)</td>
</tr>
<tr>
<td>PPID</td>
<td>0.6 (0.8)</td>
<td>0.7 (1.0)</td>
<td>0.8 (0.8)</td>
<td>1.0 (1.0)</td>
<td>1.4 (0.8)</td>
<td>1.3 (1.1)</td>
<td>1.5 (1.0)</td>
<td>0.6 (0.9)</td>
</tr>
<tr>
<td>Percentage of patients experiencing 50% pain relief</td>
<td>32.7</td>
<td>46.0</td>
<td>46.0</td>
<td>64.6</td>
<td>87.8</td>
<td>64.7</td>
<td>76.5</td>
<td>25.5</td>
</tr>
</tbody>
</table>

Scores are expressed as mean (standard deviation).

TOTPAR-8 = mean total pain relief over 8 h; TOTPAR-4 = mean total pain relief over 4 h; SPID = sum of pain intensity difference (at 4 and 8 h); SPRID = summed pain relief intensity difference (at 4 and 8 h); PPR = peak pain relief; PPID = peak pain intensity difference.

* P ≤ 0.05 versus placebo using a post hoc nonparametric analysis.
† P ≤ 0.05 versus placebo using a parametric analysis.
‡ P ≤ 0.001 versus placebo using a post hoc nonparametric analysis.
§ P ≤ 0.001 versus placebo using a parametric analysis.
|| P ≤ 0.05 versus placebo.
| P ≤ 0.001 versus placebo using the Fisher least significant difference test.
Options of Analgesia

• Before we get to options lets consider the routes:
  – Topical
  – Systemic
    • Injectable: IM vs IV
    • Oral
      – IR
      – SR
    • Nasal
    • Buccal
  – Spinal

• Duration of therapy:

• WHO Pain Ladder
• “Guidelines”
• Simple Analgesics:
  – APAP, NSAIDS
• Weak Opioids:
  – Tramadol, Codeine
• Strong Opioids:
  – Morphine, Oxycodone
• Adjuncts:
  – Everything else
Opioid Deaths

Pharmacologic Options of Analgesia:

**Pain 7-10**
Step 3
Strong Opioid
(Morphine, methadone, oxycodone, fentanyl) plus common analgesics.

**Pain 4-6**
Step 2
Weak Opioid
(Tramadol or codeine) plus common analgesics.

**Pain 1-3**
Step 1
Common Analgesics
(Dipirone, paracetamol or non-steroid anti-inflammatory drugs).

Other adjuvant drugs may be associated to these analgesics, such as antidepressants and anticonvulsants, among others.

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**Figure 1 - World Health Organization Analgesic Ladder (Adapted).**

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**Figure 3.** An updated version of the 1986 WHO pain ladder. Persistent and chronic pain syndromes should be treated with long-acting opioids; rapid-onset opioids are appropriate for breakthrough pain. A fourth step has been added for “very severe” pain that can be treated with peripheral nerve blockades.

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Recent “Guidelines” for Pain Management:

- CDC: 2016
  - Guideline for prescribing Opioids for Chronic Pain
    - https://www.cdc.gov/drugoverdose/prescribing/guideline.html
- FDA:
  - Responding to patient advocates- at present creating own “Guidelines”
- Veterans Administration: 2017
- Fibromyalgia Treatment Guidelines: 2017
- Pharmacy Benefits Managers:
- Individual Chain Initiatives:
CDC Guidelines: 2 Page pdf

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC’s Guideline for Prescribing Opioids for Chronic Pain is intended to improve communication between providers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder and overdose. The Guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

1 Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

CLINICAL REMINDERS

- Opioids are not first-line or routine therapy for chronic pain
- Establish and measure goals for pain and function

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CDC Guideline: 12 main points

1- Nonpharmacologic and non opioid preferred in chronic pain
2- Establish treatment goals
3- Discuss risks and benefits
4- Immediate should be prescribed not LA/SR
5- Prescribe lowest dose possible (Avoid >90 MME/day)
6- Long term use begins withtxt of acute pain
7- Evaluate at 1-4 weeks
8- Before continuing establish plans to mitigate risk (naloxone)
9- Review PDMP for use every 3 months
10- Consider urine drug testing
11- Avoid benzos with opioids
12- Offer txt for patients with opioid use disorder
Checklist for prescribing opioids for chronic pain

For primary care providers treating adults (18+) with chronic pain ≥3 months, excluding cancer, palliative, and end-of-life care

**When CONSIDERING long-term opioid therapy**
- Set realistic goals for pain and function based on diagnosis (eg, walk around the block).
- Check that non-opioid therapies trialed and optimized.
- Discuss benefits and risks (eg, addiction, overdose) with patient.
- Evaluate risk of harm or misuse:
  - Discuss risk factors with patient.
  - Check prescription drug monitoring program (PDMP) data.
  - Check urine drug screen.
- Set criteria for stopping or continuing opioids.
- Assess baseline pain and function (eg, PEG scale).
- Schedule initial reassessment within 1-4 weeks.
- Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

**If RENEWING without patient visit**
- Check that return visit is scheduled ≤3 months from last visit.

**When REASSESSING at return visit**
*Continue opioids only after confirming clinically meaningful improvements in pain and function without significant risks or harm.*
- Assess pain and function (eg, PEG): compare results to baseline.
- Evaluate risk of harm or misuse:
  - Observe patient for signs of over-sedation or overdose risk:
    - If yes: Taper dose.
  - Check PDMP.
  - Check for opioid use disorder if indicated (eg, difficulty controlling use):
    - If yes: Refer for treatment.
- Check that non-opioid therapies optimized.
- Determine whether to continue, adjust, taper, or stop opioids.
- Calculate opioid dosage morphine milligram equivalent (MME):
  - If >50 MME/day total (≥50 mg hydrocodone; ≥33 mg oxycodone), increase frequency of follow-up; consider offering naloxone.
  - Avoid ≥90 MME/day total (≥90 mg hydrocodone; ≥60 mg oxycodone), or carefully justify; consider specialist referral.
- Schedule reassessment at regular intervals (≤3 months).

**Evidence about opioid therapy**
- Benefits of long-term opioid therapy for chronic pain not well supported by evidence.
- Short-term benefits small to moderate for pain; inconsistent for function.
- Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.

**Non-opioid therapies**
- Use alone or combined with opioids, as indicated:
  - Non-opioid medications (eg, NSAIDs, TCAs, SNRIs, anti-convulsants).
  - Physical treatments (eg, exercise therapy, weight loss).
  - Behavioral treatment (eg, CBT).
  - Procedures (eg, intrarticular corticosteroids).

**Evaluating risk of harm or misuse**
**Known risk factors include:**
- Illegal drug use, prescription drug use for nonmedical reasons.
- History of substance use disorder or overdose.
- Mental health conditions (eg, depression, anxiety).
- Sleep-disordered breathing.
- Concurrent benzodiazepine use.

**Urine drug testing:** Check to confirm presence of prescribed substances and for undisclosed prescription drug or illicit substance use.

**Prescription drug monitoring program (PDMP):** Check for opioids or benzodiazepines from other sources.

**Assessing pain & function using PEG scale**
PEG score = average 3 individual question scores (30% improvement from baseline is clinically meaningful)

Q1: What number from 0-10 best describes your pain in the past week?
- 0 = “no pain”, 10 = “worst you can imagine”

Q2: What number from 0-10 describes how, during the past week, pain has interfered with your enjoyment of life?
- 0 = “not at all”, 10 = “complete interference”

Q3: What number from 0-10 describes how, during the past week, pain has interfered with your general activity?
- 0 = “not at all”, 10 = “complete interference”

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# VA/DoD

**VA/DoD CLINICAL PRACTICE GUIDELINE FOR OPIOID THERAPY FOR CHRONIC PAIN**

<table>
<thead>
<tr>
<th>Long Acting/ER Opioids¹</th>
<th>Initial Dosage (in opioid-naive, unless specified)</th>
<th>Other Dosing Information</th>
<th>Dosing In Special Populations</th>
<th>Other Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphine CR or SR</strong></td>
<td>Morphine CR or SR 15 mg every 8 to 12 hr administration</td>
<td>Morphine CR or SR tablets should be swallowed whole, not broken, chewed, or crushed</td>
<td>Information applies to all formulations of morphine listed</td>
<td>Morphine SR is preferred first-line long-acting agent because of similar efficacy to other long-acting opioids, comparable safety profile, provider familiarity with use, and lower cost</td>
</tr>
<tr>
<td>Available in 15, 30, 60, 100, and 200 mg strengths for every 8 to 12 hr administration</td>
<td>Total daily increments of &lt;20 to 40 mg/d may be made every 2 days</td>
<td>Elderly: Use with caution and at lower dose</td>
<td>M6G, an active metabolite, may accumulate in renal impairment and contribute to excessive opioid effects</td>
<td></td>
</tr>
<tr>
<td>Morphine ER capsules available in 10, 20, 30, 40, 50, 60, 70, 80, 100, 130, 150, and 200 mg capsule strengths for once daily administration</td>
<td><strong>Opioid-naive patients</strong>: Morphine ER capsules may be opened and the pellets may be sprinkled onto a small amount of soft food (for administration without chewing) or administered via 16F gastrostomy tube</td>
<td>Patients with renal dysfunction: Bioavailability is increased and clearance is decreased; metabolites M3G and M6G accumulate significantly</td>
<td>M3G, a metabolite without analgesic activity, may accumulate in renal impairment; this metabolite has been implicated in morphine-induced neurotoxicity, hyperalgesia, and addiction</td>
<td></td>
</tr>
<tr>
<td><strong>Opioid-naive patients</strong>: Morphine ER capsules are not indicated in opioid-naive patients</td>
<td>Steady state achieved with morphine ER within 24 to 36 hr</td>
<td>Reduce dose or, if severe renal impairment exists, avoid use</td>
<td>Morphine/naltrexone ER capsule has abuse deterrent labeling related to potential to precipitate withdrawal if drug is taken by other than oral route</td>
<td></td>
</tr>
<tr>
<td><strong>Patients who are not opioid tolerant</strong>: Start morphine ER at 30 mg daily, may adjust every 1 to 2 days</td>
<td>Morphine/naltrexone must be swallowed whole or the contents of the capsule sprinkled on apple sauce; crushing, dissolving, or shaking pellets may cause a fatal overdose (particularly in the opioid-naïve patient) and the absorption of naltrexone could increase the risk of precipitating withdrawal in opioid tolerant patients</td>
<td>Patients with hepatic dysfunction: Clearance decreases and half-life increases; M6G and M6G to morphine ratios are reduced; use carefully in patients with cirrhosis and consider reducing dose or extending dosing interval by 1.5 to 2 times</td>
<td>Morphine/naltrexone ER capsule</td>
<td></td>
</tr>
<tr>
<td><strong>Morphine and Naltrexone ER Capsule</strong></td>
<td>Initiate at the lowest dose, 20 mg/0.8 mg once daily</td>
<td>Elderly: Use with caution and at lower dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Available as 20/0.8, 30/1.2, 40/1.6, 50/2.0, 60/2.4, 80/3.2, and 100/4 capsule strengths (mg morphine/mg naltrexone) for once or twice-daily administration</td>
<td><strong>Opioid tolerant patients</strong>: Convert current opioid to equianalgesic daily dose of morphine; reduce the calculated amount by 15-50% for initial start dose (see Table D-1)</td>
<td>Patients with renal dysfunction: Bioavailability is increased and clearance is decreased; metabolites M3G and M6G accumulate significantly</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dose may be up titrated no more frequent than every other day</strong></td>
<td>Morphine/naltrexone ER capsule has abuse deterrent labeling related to potential to precipitate withdrawal if drug is taken by other than oral route</td>
<td>Reduce dose or, if severe renal impairment exists, avoid use</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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[https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf](https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf)
Opioid policy changes for Medicare members effective January 1, 2019:
Effective January 1, 2019, there are two new pharmacy claims alerts for our Medicare Advantage and Medicare Part D plans.

- 7-day supply limit for opioid naïve patients
  - Medicare patients who have not filled an opioid prescription in the previous 90 days will be limited to a 7-day or less supply without pre-authorization.
  - If the pharmacy can determine a patient has a condition that exempts them from this limit, the pharmacist can submit an override code to allow the prescription to be dispensed. Exempted conditions include patients who are being treated for active cancer, have sickle cell disease-related pain, reside in a long-term care facility, or are receiving palliative or end-of-life care.
  - If the pharmacy cannot determine if the patient has an exempted condition, the pharmacist must consult with the prescriber to confirm whether the patient has an exempted condition.
  - Opioids prescribed for patients who do not have an exempted condition require pre-authorization to determine coverage beyond a 7-day supply.

- Care coordination alert
  - Medicare Part D patients who fill prescriptions with a calculated daily morphine milligram equivalent (MME) of 90 or more from more than two pharmacies and two prescribers require the dispensing pharmacist to contact the prescriber to resolve the alert.
  - The dispensing pharmacy will consult with the prescriber about clinical appropriateness. Once determined, the pharmacist can use an override code to allow the prescription to be dispensed.

Walmart and Sam’s Club will restrict initial acute opioid prescriptions to no more than a seven-day supply, with up to a 50 morphine milligram equivalent maximum per day.
The Pendulum of the 2019

• “If everyone is in agreement that the use of opioids is excessive:

• It is our responsibility to know the additional options of therapy that have shown benefit:

• And recognize the situations when one class may be more beneficial than another class!”

– rgh
# Interventions (Recommendations 5, 6, 7)

<table>
<thead>
<tr>
<th>Low Back Pain</th>
<th>Acute</th>
<th>Subacute or Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>&lt; 4 Weeks</td>
<td>&gt; 4 Weeks</td>
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<tr>
<td><strong>Self-care</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advice to remain active</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Books, handout</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Application of superficial heat</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td><strong>Pharmacologic therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Skeletal muscle relaxants</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>Antidepressants (TCA)</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Tramadol, opioids</td>
<td>•</td>
<td>•</td>
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<tr>
<td><strong>Nonpharmacologic therapy</strong></td>
<td></td>
<td></td>
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<tr>
<td>Spinal manipulation</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Exercise therapy</td>
<td>•</td>
<td></td>
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<tr>
<td>Massage</td>
<td>•</td>
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<tr>
<td>Acupuncture</td>
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<tr>
<td>Yoga</td>
<td>•</td>
<td></td>
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<tr>
<td>Cognitive-behavioral therapy</td>
<td>•</td>
<td></td>
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<tr>
<td>Progressive relaxation</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>Intensive interdisciplinary rehabilitation</td>
<td>•</td>
<td></td>
</tr>
</tbody>
</table>

*Interventions supported by grade B evidence (at least fair-quality evidence of moderate benefit, or small benefit but no significant harms, costs, or burdens). No intervention was supported by grade A evidence (good-quality evidence of substantial benefit).
Topical:

- Irritants
  - Camphor/Menthol:
  - Capsaicin:

- NSAIDS:
- OTC:
- RX:

- Caine Anesthetics:
  - OTC: up to 4%
  - RX: 5% Patch

DON’T SMELL LIKE WALTER
Application of Superficial Heat

- Heating pad
- Whirlpool
- Menthol/Camphor Irritants
  - Bengay®
  - IcyHot®
  - Tiger Balm®
- “Non-smell”
  - Salicylate (methyl)
    - Absorbed work from inside out
  - Lidocaine:
    - 5% Lidoderm® Rx
      - Patch and Generic
    - Now up to 4% OTC
- Substance P Decreasing agents
  - Capsaicin
  - Low to high concentrations
    - TID-QID to affected areas
BIGGEST thing to happen to class:
First Line Therapy: Acetaminophen/Paracetamol

- Acetaminophen
- = Tylenol®
- Scheduled improves pain
- Does not relieve swelling
  - Minimal peripheral actions
  - Central PG analgesic
- Hepatic Toxin
- NMT 4 Grams Total/day
  - 3 grams ETOH/Liver dx
  - 2 Grams Soon? - rgh
- Blood Pressure?
- Coumadin- > 2 Grams/day
- Overdose
“Think Pair Share”

- Which of the following conditions would be most appropriate to suggest a topical camphor/menthol preparation?
  - A. Dental abscess
  - B. Post surgical pain
  - C. Neuropathic pain
  - D. Muscle overuse strain
Rationale for Opioid Plus APAP

![Graph showing pain intensity difference over time for different pain levels and treatments.]

- Severe Pain: Strong opioid ± non-opioid ± adjuvant
- Moderate Pain: Weak opioid ± non-opioid ± adjuvant
- Mild Pain: Non-opioid ± adjuvant

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Tissue Damage Pain: Confined Space Pain:

• Activation of
  – “Must know physiologic cascade number Three”- rgh

• Arachidonic Acid Metabolism
  – Bone
  – Injury
  – Dental pain
  – Osteoarthritis
  – Rheumatoid Arthritis
  – Back Pain?
Acute Pain

- Most times Acute pain is tissue damage pain:
  - Steroids or Non-Steroids

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Fig. 13-18 Arachidonic acid metabolism. Five major groups of metabolites are formed: prostaglandins, prostacyclins, thromboxanes, 5-HETE, and leukotrienes. (From Ferrante FM, Vadecboncour TR, editors: Postoperative Pain Management. New York, Churchill Livingstone, 1993.)
Arachidonic Acid Inhibitors:

- Systemic Steroids:
  - Pharmacologic doses:
    - Prednisone
      - 1 mg/kg
    - Methylprednisolone
      - 1 mg/kg
    - Dexamethasone
      - 5-10 mg PO
  - Use as DIAGNOSTICS

- Intra-articular Steroids:
  - Joint space volume dependent
  - Many products differ in onset and duration

**Physiologic doses are hydrocortisone 20mg or the equivalent. Anything above is Pharmacologic:**

<table>
<thead>
<tr>
<th>Glucocorticoids</th>
<th>Equivalent Physiologic dose</th>
<th>Stress Physiologic dose</th>
<th>Anti-inflammatory Potency</th>
<th>Plasma T1/2</th>
<th>Serum T1/2</th>
<th>Mineral Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHORT ACTING:</td>
<td>3-12 HOURS</td>
<td></td>
<td></td>
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<tr>
<td>CORTISONE:</td>
<td>25</td>
<td>100-125</td>
<td>0.3</td>
<td>30</td>
<td>5-12</td>
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<tr>
<td>HYDROCORTISONE:</td>
<td>20</td>
<td>20-100</td>
<td>1</td>
<td>90</td>
<td>5-12</td>
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<tr>
<td>INTERMEDIATE:</td>
<td>18-36 HOURS</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>PREDNISONE:</td>
<td>5</td>
<td>20-25</td>
<td>4</td>
<td>60</td>
<td>12-36</td>
<td>1</td>
</tr>
<tr>
<td>PREDNISOLONE:</td>
<td>5</td>
<td>20-25</td>
<td>4</td>
<td>200</td>
<td>12-36</td>
<td>1</td>
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<tr>
<td>TRIAMCINOLONE:</td>
<td>4</td>
<td>16-20</td>
<td>5</td>
<td>100</td>
<td>12-36</td>
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<tr>
<td>METHYL PREDNISOLONE:</td>
<td>4</td>
<td>16-20</td>
<td>5</td>
<td>130</td>
<td>12-36</td>
<td>0</td>
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<tr>
<td>LONG ACTING:</td>
<td>36-54 HOURS</td>
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<tr>
<td>DEXAMETHASONE:</td>
<td>0.75 (1)</td>
<td>3-3.75 (4-5)</td>
<td>20.30</td>
<td>1300</td>
<td>36.54</td>
<td>0</td>
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<tr>
<td>BETAMETHASONE:</td>
<td>0.6</td>
<td>2.4-3</td>
<td>28.36</td>
<td>1300</td>
<td>36-54</td>
<td>0</td>
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</tbody>
</table>

*Note: Values in parentheses are for methylprednisolone.*
Examples Intra-Articular

• Triamcinolone Acetonide: Kenalog-40
  – Large Joints:
    • 20-40mg q 1-2 weeks
  – Small Joints:
    • 5-10 mg q 1-2 weeks
  – Tendon Sheaths:
    • 5-10 mg q 1-2 weeks
  – Soft tissue infiltration:
    • 10-40 mg q 1-2 weeks
  – Bursae:
    • 20-40 mg q 1-2 weeks

• Dexamethasone Acetate: Decadron LA-
  – Large Joints:
    • 4-16 mg q 1-3 weeks
  – Small Joints:
    • 1-4 mg q 1-3 weeks
  – Tendon Sheaths:
    • 1-4 mg q 1-3 weeks
  – Soft tissue infiltration:
    • 2-8 mg q 1-3 weeks
  – Bursae:
    • 2-4 mg q 1-3 weeks
## Commercially available NSAIDs

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Dosage forms</th>
<th>Interval</th>
<th>Max Daily (mg)</th>
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<td><strong>Propionic Acids:</strong></td>
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<tr>
<td>Ibuprofen</td>
<td>Advil, Nuprin, Motrin, generics</td>
<td>100 mg, 200 mg, 400 mg, 600 mg, 800 mg, 100/5</td>
<td>TID-QID</td>
<td>3,200</td>
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<tr>
<td>Fenoprofen</td>
<td>Naflon, generics</td>
<td>200 mg, 600 mg</td>
<td>TID-QID</td>
<td>3,200</td>
</tr>
<tr>
<td>Ketoprofen IR</td>
<td>Orudis, generics</td>
<td>50 mg, 75 mg</td>
<td>TID-QID</td>
<td>300</td>
</tr>
<tr>
<td>Ketoprofen SR</td>
<td>Crupall, generics</td>
<td>200 mg</td>
<td>QD (BID)</td>
<td>400</td>
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<tr>
<td>Naproxen</td>
<td>Naprosyn, generics</td>
<td>250 mg, 375 mg, 500mg</td>
<td>BID</td>
<td>1,250</td>
</tr>
<tr>
<td>Naproxen SR</td>
<td>Naproxen EC, generics</td>
<td>375 mg, 500 mg</td>
<td>BID</td>
<td>1,250</td>
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<tr>
<td>Naproxen sodium</td>
<td>Aleve, Anaprox, generics</td>
<td>220 mg, 275 mg, 550 mg</td>
<td>BID</td>
<td>1,250</td>
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<tr>
<td>Naproxen Sod ER</td>
<td>Naprelin, generics</td>
<td>375 mg, 500 mg</td>
<td>BID</td>
<td>1,250</td>
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<tr>
<td>Flurbiprofen</td>
<td>Ansaid, generics</td>
<td>50 mg, 100 mg</td>
<td>QD (BID)</td>
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<td>Oxaprozin</td>
<td>Daypro, generics</td>
<td>600 mg</td>
<td>QD</td>
<td>2,400</td>
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<td><strong>Naphthylalkanones:</strong></td>
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<tr>
<td>Nabumetone</td>
<td>Relafen, generics</td>
<td>500 mg, 750 mg</td>
<td>QD</td>
<td>2,000</td>
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<td><strong>Fenamates:</strong></td>
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<td>Metamizole</td>
<td>Ponstel, generics</td>
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<td>TID</td>
<td>1,000</td>
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<td>Meclofenamate</td>
<td>Meclofen, generics</td>
<td>50 mg, 100 mg</td>
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<td><strong>Indole Acetic Acids:</strong></td>
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<tr>
<td>Sulindac</td>
<td>Clinoril, generics</td>
<td>150 mg, 200 mg</td>
<td>BID</td>
<td>400</td>
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<tr>
<td>Indomethacin IR</td>
<td>Indocin, generics</td>
<td>25 mg, 50 mg</td>
<td>TID-QID</td>
<td>200</td>
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<tr>
<td>Indomethacin SR</td>
<td>Indocin SR, generics</td>
<td>75 mg</td>
<td>QD (BID)</td>
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<td><strong>Non-acetylatated salicylates and salicylate-like:</strong></td>
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<tr>
<td>Salicylate</td>
<td>Disacid, generics</td>
<td>500 mg, 750 mg</td>
<td>BID-TID</td>
<td>3,000</td>
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<tr>
<td>Diflunisal</td>
<td>Dafline, generics</td>
<td>250 mg, 500 mg</td>
<td>BID-TID</td>
<td>1,500</td>
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<td><strong>Phenylacetic acids:</strong></td>
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<tr>
<td>Diclofenac sodium</td>
<td>Voltaren, generics</td>
<td>25 mg, 50 mg</td>
<td>BID-TID</td>
<td>300</td>
</tr>
<tr>
<td>Diclofenac Na SR</td>
<td>Voltaren XR, generics</td>
<td>100 mg</td>
<td>QD-BID</td>
<td>300</td>
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<td>Diclofenac potassium</td>
<td>Caladon, generics</td>
<td>50 mg</td>
<td>QD-BID</td>
<td>300</td>
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<td><strong>Pyran carboxylic acids:</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Etodolac IR</td>
<td>Lodine, generics</td>
<td>200 mg, 300 mg, 400 mg, 500 mg</td>
<td>BID-TID</td>
<td>1,200</td>
</tr>
<tr>
<td>Etodolac SR</td>
<td>Lodine XL, generics</td>
<td>400 mg, 500 mg, 600 mg</td>
<td>QD (BID)</td>
<td>1,200</td>
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<td><strong>Oxidoxas:</strong></td>
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<tr>
<td>Piroxicam</td>
<td>Feldene, generics</td>
<td>10 mg, 20 mg</td>
<td>QD-BID</td>
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<tr>
<td>Meloxicam</td>
<td>Mobic, generics</td>
<td>7.5 mg, 15 mg</td>
<td>QD-BID</td>
<td>30</td>
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<tr>
<td><strong>Pyrazine carboxylic acids:</strong></td>
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<tr>
<td>Ketonolac</td>
<td>Toradol, generics</td>
<td>10 mg</td>
<td>SID NMT 5D</td>
<td>50</td>
</tr>
<tr>
<td><strong>Cox-2 selective:</strong></td>
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</tr>
<tr>
<td>Celecoxib</td>
<td>Celebrex</td>
<td>100 mg, 200 mg, 400 mg</td>
<td>QD-BID</td>
<td>400</td>
</tr>
</tbody>
</table>
Acute Pain NSAID Recommendations:

- **Ketorolac Toradol®**
  - 10 mg 5ID x 5 days (4 days)

- **Indomethacin Indocin®**
  - 50 mg TID

- **Naproxen Sodium Anaprox®**
  - 550 mg BID

- **Ibuprofen Motrin®**
  - 800 TID

- **Sulindac Clinoril®**
  - 200 mg BID

- **Diclofenac Potassium Cataflam®**
  - 50 mg TID

**Schedule for first week**

- Then back down to lowest dose best tolerated agent

- Not everyone needs COX-2 walking in door!
Adverse Events NSAIDS

- Cardiovascular:
  - Hypertension
    - How to Identify?
  - Heart Failure
    - How to Identify?
  - Renal Failure

- Hepatic Toxins
  - How to Identify?

- Bone Marrow Supp
  - How to Identify?

- Worsen Asthma
  - “Must know physiologic cascade three”
  - Why?
  - How to identify
Adverse Events NSAIDS

- Gastrointestinal
  - Upper:
    - Gastritis
  - Stomach:
    - Decrease PG
    - Decrease Bicarb
    - Decrease Mucus
      - Decrease Viscosity
    - Peptic Ulcer Disease
  - Lower:
    - Abdominal Distress

What do we do if they MUST stay on NSAID and have had a bleed?
“Think Pair Share”

• Which of the following conditions would be most appropriate to suggest a medication that has inhibition of arachidonic acid metabolism characteristics?
  – A. Dental abscess
  – B. Post surgical pain
  – C. Neuropathic pain
  – D. Muscle overuse strain
Must need NSAIDS and Bleed

- Add Prostaglandins
  - Misoprostil
    - Cytotec® 100 200 mcg
      - TID to QID
    - To any of them
- Or
- Arthrotec® 50/200,75/200
  - Diclofenac + Misoprostil

Nambumetone
  - Relafen®
    - 500-2250 mg q day

Cox-2
  - Celecoxib Celebrex®
  - Meloxicam Mobic®

Or:
Treat while causing
Proton Pump Inhibitors
H2 Blockers
And when we run out of oral routes:
**Rx- Diclofenac Topical**

**Table 3. Efficacy Outcomes of Voltaren® Gel in Studies 1 and 2**

<table>
<thead>
<tr>
<th></th>
<th>Voltaren® Gel</th>
<th>Placebo (Vehicle)</th>
<th>Adjusted Difference (Placebo - Voltaren® Gel)</th>
</tr>
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<tbody>
<tr>
<td><strong>Study 1 (Knee)</strong></td>
<td></td>
<td></td>
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<tr>
<td>WOMAC Pain* at Week 12</td>
<td>127</td>
<td>119</td>
<td>Δ = 7′</td>
</tr>
<tr>
<td>Sample Size</td>
<td>28</td>
<td>37</td>
<td>(1, 12)</td>
</tr>
<tr>
<td>Mean Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study 2 (Hand)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Intensity at Week 4</td>
<td>198</td>
<td>187</td>
<td>Δ = 7″</td>
</tr>
<tr>
<td>Sample Size</td>
<td>43</td>
<td>50</td>
<td>(2, 12)</td>
</tr>
<tr>
<td>Mean Outcome</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study 2 (Hand)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Intensity at Week 6</td>
<td>198</td>
<td>187</td>
<td>Δ = 7″</td>
</tr>
<tr>
<td>Sample Size</td>
<td>40</td>
<td>47</td>
<td>(1, 13)</td>
</tr>
<tr>
<td>Mean Outcome</td>
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<td></td>
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<tr>
<td>95% Confidence Interval</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* WOMAC = Western Ontario McMaster Osteoarthritis Index.

# Scale from 0 (best) to 100 (worst).

† Difference is adjusted using an analysis of covariance (ANCOVA) model with main effects of treatment and center and baseline covariate.

†† Difference is adjusted using an analysis of covariance (ANCOVA) model with main effects of treatment, center, indicator for pain in the CMC-1 joint, and baseline as a covariate, and the treatment-by-CMC-1 indicator interaction. Difference is weighted by size of CMC-1 strata.

4 grams QID
100 Gram Tube = 6.25 Days
5 Tubes = 1 month
AWP- $199.01
-vs-
Diclofenac Sodium 75 mg DR
BID-#60
$4.00
**Neuropathic Pain: Fibromyalgia:**

Update on Treatment Guideline in Fibromyalgia Syndrome with Focus on Pharmacology

<table>
<thead>
<tr>
<th>Drug</th>
<th>Contraindications</th>
<th>Warning and Precautions</th>
<th>Last Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Prior Hypersensitivity / Concomitant use of MAOI / Acute recovery phase following myocardial infarction / Mania / Severe liver disease / Congestive heart failure</td>
<td>Suicidality / Hypotension / QT interval prolongation on ECG / Blood dyscrasias</td>
<td>5 December 2016</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Serotonin syndrome and MAOIs / Concomitant use of irreversible MOAIs, fluvoxamine, ciprofloxacin or enoxacin / Liver disease resulting in hepatic impairment / Severe renal impairment</td>
<td>Mania and seizures / Mydriasis / Hypertension / Renal impairment / Serotonin syndrome suicide / Diabetic peripheral neuropathic pain / Hypotenaesia</td>
<td>8 February 2008</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Known hypersensitivity to pregabalin (PGB) or any of its components</td>
<td>- Hypersensitivity reaction / Dizziness, somnolence, loss of consciousness / Vision-related effects / Increase risk of suicidal thoughts and behaviours / Encephalopathy / Reduced lower gastrointestinal tract function</td>
<td>14 November 2016</td>
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<tr>
<td>Tramadol Hydrochloride</td>
<td>Hypersensitivity to tramadol or other opioids / Severe hepatic/renal impairment MOA or within 2 weeks of their withdrawal</td>
<td>Withdrawal symptoms / Dependence and abuse / Convulsive disorders</td>
<td>22 September 2015</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>Hypersensitivity / Concomitant use to MAOI / Liver disease resulting in hepatic impairment / Uncontrolled hypertension / Severe renal impairment</td>
<td>As per Duloxetine</td>
<td>8 February 2017</td>
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</tbody>
</table>
SNRIs/TCAs

ARIs Amine Reuptake Inhibitors

- TCAs
- Tetracyclics
- “SSRI’s”
- “SNRI’s”
- Miscellaneous
- MAO Inhibitors
<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Dosage Forms</th>
<th>Starting Dose</th>
<th>Max Dose</th>
<th>5-h</th>
<th>NE</th>
<th>Anti hist</th>
<th>Antich</th>
<th>Sed</th>
<th>Dry</th>
<th>Hypo</th>
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<tbody>
<tr>
<td>Clomipramine</td>
<td>Anafranil® Generics</td>
<td>25, 50, 75mg</td>
<td>25 HS-TID</td>
<td>250</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++++</td>
<td>+++</td>
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<tr>
<td>Amiriptyline</td>
<td>Elavil® Endep® Generics</td>
<td>10, 25, 50, 100, 150</td>
<td>10 HS- 150 HS</td>
<td>300</td>
<td>+++</td>
<td>+++</td>
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<td>Imipramine</td>
<td>Tofranil® Generics</td>
<td>10, 25, 50</td>
<td>10 HS</td>
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<td>+++</td>
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<td></td>
<td>Tofranil PM®</td>
<td>75, 100, 125, 150</td>
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<td>Doxepin</td>
<td>Sinequan® Adapin® Generics</td>
<td>10, 25, 50, 100, 150</td>
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<td>300</td>
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<td>+</td>
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<td>Trimipramine</td>
<td>Surmontil®</td>
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<td>+</td>
<td>+++</td>
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<td>Maprotyline</td>
<td>Ludimil® Generics</td>
<td>25, 50, 75</td>
<td>25 HS</td>
<td>225</td>
<td>0/+</td>
<td>++</td>
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<td>++</td>
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<td>Mirtazapine</td>
<td>Remeron®</td>
<td>15, 30, 45</td>
<td>15 HS</td>
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<td>+++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
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<td>Amoxapine</td>
<td>Ascendin® Generics</td>
<td>25, 50, 100, 150</td>
<td>25 HS</td>
<td>600</td>
<td>++</td>
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<td>Nortriptyline</td>
<td>Pameler® Aventyl® Generics</td>
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<td>++</td>
<td>+++</td>
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<td>++</td>
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<td>Desipramine</td>
<td>Norpramin® Pertrofane® Generics</td>
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<td>+++</td>
<td>++</td>
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<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
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</tbody>
</table>
“Old Pharmacology New Spin”

• “Depression Hurts”
• “SNRI”
  – Duloxetine Cymbalta®, Gen
  – Venlafaxine Effexor®, Gen
  – Desvenlafaxine Pristiq® Gen
  – Milnacipran Savella® Gen
  – Levomilnacipran Fetzima®
ARI/Opioid

- Tramadol Ultram®
- C-IV
- NMT 8/day

Tapentadol Nucynta

- Mu-opioid receptor agonist
- Norepinephrine reuptake inhibitor
- 50, 75, 100 mg tablets NMT 600/day
- Oral bioavailability 32%, T ½ 4 hours
- 97% hepatic metabolism Renal elimination
- 100 Q 6 hours
- C-II !!!
- Analgesia comparable to Oxycodone,

Tramadol Comparative Potency:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mu</th>
<th>Delta</th>
<th>Kappa</th>
<th>NE</th>
<th>5-HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>2.1</td>
<td>57.6</td>
<td>42.7</td>
<td>0.79</td>
<td>0.99</td>
</tr>
<tr>
<td>M1 Metab</td>
<td>0.012</td>
<td>0.91</td>
<td>0.24</td>
<td>1.52</td>
<td>5.18</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.0003</td>
<td>0.09</td>
<td>0.057</td>
<td>IA</td>
<td>IA</td>
</tr>
<tr>
<td>Codeine</td>
<td>0.2</td>
<td>5.1</td>
<td>6.0</td>
<td>IA</td>
<td>IA</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>0.034</td>
<td>0.38</td>
<td>1.22</td>
<td>IA</td>
<td>IA</td>
</tr>
<tr>
<td>Imipramine</td>
<td>3.7</td>
<td>12.7</td>
<td>1.8</td>
<td>0.0066</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Lower the Value of Kᵢ, the higher the affinity
Alpha2-Delta Subunit Calcium Channel

- Neurontin® Gabapentin
- Lyrica® Pregabalin

Figure 1. Chemical structures of gabapentin and pregabalin.

Role of spinal voltage-dependent calcium channel α₂ß-1 subunit in the expression of a neuropathic pain-like state in mice.
Gabapentin

• Though the mechanism of action of gabapentin in the treatment of neuropathic pain is not clear, it does not influence the same pathways as opioids or tricyclic depressants. Current evidence indicates that gabapentin affects voltage-gated calcium channels in the CNS.

• Gabapentin binds to the $\alpha 2\delta$ subunit of the voltage-dependent calcium channel, regulating the action of the calcium channels and neurotransmitter release.
Pregabalin Efficacy DPN
Diabetic Peripheral Neuropathy

Figure 1: Patients Achieving Various Levels of Pain Relief – Study DPN 1

Fibromyalgia: 20% patients will get 50% reduction
Membrane Stabilizing Works Well
“BIG 4” Keppra may also be tried

- **Barbiturates:**
  - Phenobarbital
    - 30-90mg a day

- **Valproic Acid**
  - Depekene®
  - Depakote®
  - Depakote ER®
    - Liver
    - BM
    - Weight Gain
    - Hyperammonemia

- **Carbamazepine:**
  - Tegretol®, Generics
  - XR®, Carbatrol®
    - Liver
    - BM

- **Phenytoin:**
  - Dilantin
    - Liver
    - BM
    - Gingival Hyperplasia
    - Skin Warnings 11/2008

Everything else is a “me to”: Mesantoin, Zarontin, Celontin, Benzos, Trileptal, Felbatol, Lamictal, Zonagran, Topamax, Keppra, Gabitril
“Think Pair Share”

• Which of the following conditions would be most appropriate to suggest a medication that has both NE and Serotonin increasing properties?
  – A. Dental abscess
  – B. Post surgical pain
  – C. Neuropathic pain
  – D. Muscle overuse strain
Muscle Relaxants: Role?

• Chlorzoxazone:
  – Parafon Forte®
  – 500 mg TID-QID
• Carisoprodol:
  – Soma®
  – 350 mg TID-QID
• Cyclobenzaprine:
  – Flexeril®
  – 10 mg TID-QID
  – Please never:
    • Flexeril® 5 mg
    • SR Amrix® 15 mg
• Metaxolone:
  – Skelexin®
  – 400 mg TID-QID
• Methocarbamol:
  – Robaxin®
  – 500, 750 mg TID-QID
• Orphenadrine:
  – Norflex®
  – 100mg BID-TID
• Tizanidine
  – Zanaflex®
  – 4-8 mg TID-QID
Muscle Relaxants

• Carisoprodol Better than Diazepam at 7 days
  – 70% improvement VAS vs 45%
• Carisoprodol Equal to Cyclobenzaprine at 8 days
  – VAS Improvement 30mm vs 28 mm
• Tizanidine Better than Diazepam on Pain at 7 days
  – 77% improvement vs 47%
  – No difference in functionality 87% vs 93%
GABA Receptor Agonists/Benzos

Strong Guideline recommendations to NOT use with opioids: Deaths dramatically increased with the combination!

<table>
<thead>
<tr>
<th>Anxiolytics:</th>
<th>Hypnotics: (sleeping pills)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic:</strong></td>
<td><strong>Trade:</strong></td>
</tr>
<tr>
<td><strong>Diazepam</strong></td>
<td>Valium®, Gen</td>
</tr>
<tr>
<td><strong>Chlordiazepoxide</strong></td>
<td>Librium®, Gen</td>
</tr>
<tr>
<td><strong>Oxazepam</strong></td>
<td>Serax®, Gen</td>
</tr>
<tr>
<td><strong>Chlorazepate</strong></td>
<td>Tranxene®, Gen</td>
</tr>
<tr>
<td><strong>Lorazepam</strong></td>
<td>Ativan®, Gen</td>
</tr>
<tr>
<td><strong>Alprazolam</strong></td>
<td>Xanax®, Xanax XR®, Generics</td>
</tr>
<tr>
<td><strong>Clonazepam</strong></td>
<td>Klonipin®, Gen</td>
</tr>
<tr>
<td><strong>Halazepam</strong></td>
<td>Paxipam®, (Off Market)</td>
</tr>
<tr>
<td><strong>Prazepam</strong></td>
<td>Cenrex®, (off market)</td>
</tr>
</tbody>
</table>

---

*Source:* [Idaho State University](https://www.isu.edu)
“Narcotics”
"Med Chem is Important"

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Dose Available</th>
<th>Onset</th>
<th>Duration</th>
<th>IV</th>
<th>IM</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phenethrines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine Sulfate</td>
<td>Many MS Contir® Kadian® Avinza® Oramorph®</td>
<td>IR: 15, 30, 60 10/5,20/5 Conc-20/1ml SR: 15,30,60, 100,200 30,60,90,120 10mg supp</td>
<td>15-60</td>
<td>2-4</td>
<td>2-4</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Dilaudid® Palladone 2005-SR Exalgo®</td>
<td>1,2,3,4, 8 mg tab 3 mg supp 8,12,16,32</td>
<td>15-30</td>
<td>4-5</td>
<td>1</td>
<td>1.5</td>
<td>2-4</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Numorphan- INjec Opana® po Opana ER®</td>
<td>1,1.5/ml 5, 10 IR 5,10,20,30,40 SR</td>
<td>5-10</td>
<td>3-6</td>
<td>0.5</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Oxycodone IR- 5,10,15,20, 30 APAP- 2.5,5,7.5,10</td>
<td>Roxicodone Tylox, Percodan, Percocet SR- Oxycontin®</td>
<td>5 po, 7.5,10 5/5 ml, 20/ml 10,15,20,30,40,60, 80</td>
<td>15-30</td>
<td>4-6</td>
<td>na</td>
<td>na</td>
<td>20</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Many plus apap, asa, ibu</td>
<td>2.5,5,7.5,10</td>
<td>15-60</td>
<td>3-6</td>
<td>na</td>
<td>na</td>
<td>40 (20-30)</td>
</tr>
<tr>
<td>Codeine</td>
<td>Many plus apap, prom, guaif</td>
<td>15,30,60</td>
<td>10-30</td>
<td>3-6</td>
<td>na</td>
<td>120</td>
<td>180</td>
</tr>
</tbody>
</table>
**“Non-phenanthrenes”**

<table>
<thead>
<tr>
<th><strong>Morphinans</strong></th>
<th><strong>Generic</strong></th>
<th><strong>2mg po</strong></th>
<th><strong>60</strong></th>
<th><strong>6-8</strong></th>
<th><strong>1</strong></th>
<th><strong>2</strong></th>
<th><strong>4</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Levorphanol</td>
<td>Generic</td>
<td>1, 2mg/ml Im, 10mg/ml NS</td>
<td>10-15</td>
<td>2-3</td>
<td>0.5-1</td>
<td>4</td>
<td>na</td>
</tr>
</tbody>
</table>

**Phenylheptylamines:**

| **Methadone** | **Dolophin®** | **po, iv, pr, im 5, 10, 40mg 5,10/5 soln 10/1 conc 10/1 ml inj** | **30-60** | **6-8** | **5** | **10** | **10** |

| **Propoxyphene** | **Darvon (ceft)** | **po** | **30-60** | **3-4** | na | na | **200** |

**Phenylpiperidines:**

| **Meperidine** | **Demerol®** | **po, iv im 25,50,75,100/ml 50,100 mg tabs** | **15-30** | **3-4** | **50** | **75** | **200** |

| **Fentanyl** | **Sublimaze® inj Duragesic® top Actiq® loz Fentora® Oral** | **12.5, 25,50, 75, 100 MCG/hour 1,2,3,4,6,800 loz 0.05/ml inj 1,2,3,4,6,800 oral** | **5-10** | **1-2** | **0.05** | **0.1** | **100 mcg** |
“Abuse Potential”

• “Once you get Hydromorphone Dilaudid®- you never go back!!!- rgh
• Oxycodone-
  – Sustained Release Oxycontin®
  – Immediate Release, Ir
• Oxymorphone- Opana®
  – Sustained Release Opana ER®
  – Immediate Release
• REMS- Abuse Deterrent Tablets
Naloxone:

- **IM:**
  - 0.4mg SDV AWP $18.00
- **IV:**
  - Establishing Access- lay person?
- **Nose Spray:**
  - 4 mg AWP $150.00/ 2 pack

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Surgeon General’s Advisory on Naloxone and Opioid Overdose

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life.

BE PREPARED. GET NALOXONE. SAVE A LIFE.
“Cutting Edge”
Prior to the Procedure

• What has been shown when given pre-operatively or pre procedure to decrease post procedure analgesic requirements?

• Dexamethasone
• Ibuprofen
• Diclofenac
• Celecoxib
• Acetaminophen
• Gabapentin

Study:
Nanzawa A, et.al Anesh Prog 2018 65:24-29 Dental Extraction Population

APAP 1000 mg Group A
Placebo Group P
Celecoxib 400 mg Group C
Diclofenac 50 mg Group D
Hanzawa Results Pre-operative drug with post operative analgesia

Figure 1. Box plots for visual analog scale (VAS) scores at 4, 5, and 6 hours after administration of study drug. Data are expressed as medians, percentiles, and ranges. *p < .05 compared with the placebo group; **p < .01 compared with the placebo group by Kruskal-Wallis H test and Mann-Whitney U test with Bonferroni correction.

Figure 2. Consumption of fentanyl up to 4, 5, and 6 hours after administration of study drug. Data are expressed as mean ± SD. *p < .05 compared with the placebo group; **p < .01 compared with the placebo group by non-repeated-measures analysis of variance and Student-Newman-Keuls test.

Nanzawa A, et.al Anesh Prog 2018 65:24-29
Low Dose Naltrexone: Fibromyalgia Pain:

Figure 1. Outline of the study protocol.
Low dose Ketamine: Pain Syndromes

### ER: Acute Pain Interventions

<table>
<thead>
<tr>
<th>Dose</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 – 0.3 mg/kg</td>
<td>Analgesia</td>
</tr>
<tr>
<td>0.2 – 0.5 mg/kg</td>
<td>Recreational</td>
</tr>
<tr>
<td>0.4 – 0.8 mg/kg</td>
<td>Partially dissociated</td>
</tr>
<tr>
<td>1-2 mg/kg</td>
<td>Fully dissociated</td>
</tr>
</tbody>
</table>

**Ketamine- Faster acting yet shorter duration = Another potential option**

### Primary Outcome

<table>
<thead>
<tr>
<th>Measure</th>
<th>Ketamine (baseline score)</th>
<th>Morphine (baseline score)</th>
<th>Mean difference (95% C.I.)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pain score at 30 minutes</td>
<td>4.1 (8.6)</td>
<td>3.9 (8.5)</td>
<td>0.2 (-1.19 to 1.46)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

C.I = confidence interval, p = probability

### Secondary Outcomes

<table>
<thead>
<tr>
<th>Measure</th>
<th>Ketamine</th>
<th>Morphine</th>
<th>% difference (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for rescue analgesia at 30 min</td>
<td>9%</td>
<td>2%</td>
<td>7% (3 to 16)</td>
</tr>
<tr>
<td>Need for rescue analgesia at 60 min</td>
<td>9%</td>
<td>14%</td>
<td>-5% (-18 to 9)</td>
</tr>
<tr>
<td>Any adverse effect postinjection</td>
<td>73%</td>
<td>51%</td>
<td>22% (2 to 42)</td>
</tr>
<tr>
<td>Any adverse effect at 30 minutes</td>
<td>36%</td>
<td>33%</td>
<td>3% (-18 to 22)</td>
</tr>
</tbody>
</table>

### Post hoc analysis

<table>
<thead>
<tr>
<th>Measure</th>
<th>Ketamine</th>
<th>Morphine</th>
<th>% difference (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete resolution of pain at 15 minutes</td>
<td>44%</td>
<td>13%</td>
<td>31% (13 to 49)</td>
</tr>
<tr>
<td>Complete resolution of pain at 30 minutes</td>
<td>27%</td>
<td>24%</td>
<td>3% (-16 to 21)</td>
</tr>
<tr>
<td>Need for rescue analgesia at 120 minutes</td>
<td>29%</td>
<td>12%</td>
<td>17% (1 to 34)</td>
</tr>
</tbody>
</table>

2015; Annals of Emergency Medicine; 66(3) 222-229
Cannabinoids:

• Can of worms but it works

Best marijuana strains for chronic pain

The different types of marijuana plants include the following:

• *Cannabis indica*

• *Cannabis sativa*

• hybrids

There is limited research available on the use of specific marijuana strains for pain and other symptoms. As a result, strain-specific recommendations are not medically proven.

The results of an online survey, comprising 95 participants, featured in the *Journal of Alternative and Complementary Medicine* in 2014.
Newer Pain Buzz

- Vitamin D
- Correlations:
- Efficacy?
- Natraceuticals:
  - Kratom
  - Turmeric
  - Glucosamine
  - Dozens others

Nowson CA, Margerison C. Vitamin D intake and vitamin D status of Australians. *MJA.* 2002; 177 (3) : 149-152.
Chronic Pain Patient’s Self Perception:

Fig. 4-4  A, An organic pain drawing. Note the well localized, anatomically plausible distribution of pain. B, A nonorganic pain drawing. Note the widespread, poorly defined pattern of pain distribution. (From Udén A, Åström M, Bergenudd H: Pain drawings in chronic back pain. Spine 13:389-392, 1988.)
The End