From Multimodal Analgesia, Magic to Methadone: Taming of the Shrew

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April 1, 2020:
Center of Pain Medicine, Palliative Care and Integrative Medicine

Learning Objectives

• Discuss “Multimodal Analgesia” - how multiple agents, interventions, rehabilitation, psychological and integrative (“non-pharmacologic”) therapies act synergistically for more effective pediatric pain control with fewer side effects than any single analgesic or modality
  • Review advantages and disadvantages in methadone administration
  • Evaluate potential adverse effects of methadone & difference of half-life compared to other opioids
  • Practice opioid rotation to methadone in a case example
5-year old Marius: Procedural Pain Management

Don't have enough staff for pediatric pain control...?

Funny, how there is always enough staff to restrain a child.

Mathew Crawford, MD, Sydney Children's Hospital, Australia

Positioning

- Use of Restraint Never Supportive: Restraining children for procedures makes them feel ashamed, humiliated, powerless; report having lost right to control his/her own body

Positioning
**Children with progressive, non-curable genetic, metabolic, or neurological conditions**

- 275 children with progressive, non-curable genetic, metabolic, or neurological conditions: **Pain 53% [Most of the time: 21.8%]**


**So, how do we treat the individual pain patient with serious illness in front of us?**

*Hmhh...*  
Spoiler Alert: Crystal-clear answer on 3rd last slide!
So…if pain rated 8/10…
what are we measuring…?

1. **Acute Somatic Pain**: arises from activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation [e.g. localized, sharp, squeezing, stabbing, or throbbing]
   - Somatic (for example, muscles, joints)
   - Chronic somatic pain typically well localized & often results from degenerative processes (such as arthritis)

2. **Total Pain**: suffering that encompasses all of a child’s physical, psychological, social, spiritual, and practical struggles

3. **Neuropathic Pain**: resulting from injury to, or dysfunction of, the somatosensory system. [burning, shooting, electric, or tingling]
   - Central pain: caused by a lesion or disease of the central somatosensory nervous system

4. **Visceral Pain**: results from activation of nociceptors of thoracic, pelvic, or abdominal viscera [e.g. poorly localized, dull, crampy, or achy]

5. **Chronic Postsurgical Pain (CPSP)**

6. **Chronic (Persistent) Pain**: 
   - Pain beyond expected time of healing

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**PAIN** → **BRAIN**

Rene Descartes 1596-1650

John Lieff: Are Microglia the Most Intelligent Brain Cells? http://jonlieffmd.com/blog/are-microglia-the-most-intelligent-brain-cells
What are children most afraid of when coming to see a doctor?

Changing Culture

Attitudes:
• Needle sticks don’t hurt that much
• The pain of a needle stick is unavoidable…

“Hold them down and do it quick…”
“Just get it the first time!”

Essential Components of Needle Pain Prevention

4 Simple Steps
• Topical Anesthesia
• 0-12 months: Sucrose / Breastfeeding
• Positioning
• Distraction (Integrative “non-pharmacological” therapies)

Develop Plan B (or deferral process)
• Child life, psychology
• Nitrous gas sedation
• Consider moderate-deep sedation, if excellent analgesia cannot be achieved
• other approaches

“Toyota Lean Value Stream” plus “Influencer”:

Children’s COMFORT PROMISE
We will do everything possible to prevent and treat pain.

WHAT IF GETTING SHOTS DIDN’T HURT?
Multimodal Analgesia

No Needless Pain

That's why we're called

No Needless Pain The Children's Comfort Promise
https://vimeo.com/20329079

A hospital-wide initiative to eliminate or reduce needle pain in children using lean methodology

Stefan J. Friedrichsdorf***, Donna Eulf*, Christian Weidner*, Andrea Postier*

PAIN Reports 2018. (3)e671

https://journals.lww.com/painrpts/Fulltext/2018/09001/A_hospital-wide_initiative_to_eliminate_or_reduce_9.aspx

Ow! I didn't feel it @childrensmn
ComfortPromise: numb the skin, sitting upright & distract
childrensMN.org/comfortpromise
**Basic Analgesics**

- Acetaminophen (Paracetamol)
- NSAIDs / COX-2 Inhibitor

**Pediatric Multimodal Analgesia**

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**Citius, Altius, Fortius...?**

- Ibuprofen salts: fast-acting formulations
  - Advil® Film-Coated Tablets, contains 266 mg of ibuprofen sodium (equivalent to 200 mg of standard ibuprofen)
  - Produced significantly better analgesia over 6h, fewer re-medications than standard formulations
  - 200-mg fast-acting ibuprofen (NNT 2.1; 95% confidence interval 1.9-2.4) was as effective as 400 mg standard ibuprofen (NNT 2.4; 95% CI 2.2-2.5), with faster onset of analgesia.

- More rapid absorption, faster initial pain reduction, good overall analgesia in more patients at the same dose, and probably longer-lasting analgesia, but with no higher rate of patients reporting adverse events.

- However, earlier onset preferred in other pain condition, such as chronic nociceptive or neuropathic pain.

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**Celecoxib & bleeding**

- At supratherapeutic doses (600mg BID), celecoxib not interfering with normal mechanisms of platelet aggregation / hemostasis

- COX-2 inhibitors not increasing risk of intraoperative, postoperative bleeding, or blood loss; no significant effect on platelet function. Therefore, perioperative, single dose, or short course of COX-2 inhibitors can be safely used in individuals undergoing surgery.

- COX-2 inhibitors significantly reduced the risk of perforation, obstruction, bleeding, diarrhea, and withdrawal due to GI adverse events
**Pediatric Multimodal Analgesia**

**Basic Analgesics**
- Acetaminophen (Paracetamol)
- NSAIDs / COX-2 Inhibitor

**Opioids**
- Tramadol (“weak”)
- Morphine (“strong”)
- Fentanyl, Hydromorphone, Oxycodone, Methadone (UK: Diamorphine)

**4 WHO Principles**
- “By the Clock”
- Multimodal (Opioid-sparing) Analgesia

**WHO Principle 4: Using a Two-Step Strategy**

**WHO Step 1: Mild Pain**
- Ibuprofen and/or Acetaminophen (Paracetamol)
- Other NSAIDs? Cox-2 Inhibitor?

**WHO Step 2: Moderate to Severe Pain**
- Tramadol
- Low-dose Opioid
- Codeine
- Hydrocodone

**Morphine**
- or fentanyl, hydromorphone, oxycodone, methadone (UK: diamorphine)

“How many children have to suffer needlessly from pain to avoid one opioid death?”
Advantages & Disadvantages of Methadone?

Methadone: Advantages?
- Long acting
- Very effective in chronic pain relief
- Effective in neuropathic pain
- NMDA receptor blocker (helps preventing tolerance)
- Rapid onset of action (!)
- Lower incidence of constipation
- No active metabolites
- Safe in renal failure
- Safe in stable liver disease
- Incomplete cross tolerance (!)
- Inexpensive

Methadone: Disadvantages?
- Long half-life (may lead to accumulation; quick titration difficult)
- Wide dosing variation
- Equianalgesic conversion more complex
- Stigma?
Methadone

Routes of Administration
- Oral
- Sublingual (if concentrated)
- Rectal
- Intravenous
- Subcutaneous

Adverse effects
- Sedation, nausea, constipation
- Higher doses: opioid-induced neurotoxicity (myoclonus, hallucinations, nightmares), respiratory depression
- Hypoglycemia during rapid methadone dose escalation
- Hypoglycemia increased from 3.7 to 6.9% of patient days [of those 3% <40mg/dL/2.2 mmol/L] (>80% also other opioids)

Methadone

2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidene (EDDP) (pharmacologically inactive)
2-ethyl-5-methyl-3,3-diphenyl-1-pyrroline (EMDP) (pharmacologically inactive)
Methadole and Normethadole (minor activity)

Mechanism of Action
- \(\mu, \delta, \kappa\) - opioid receptor agonist (L \([R-]\)-methadone)
- NMDA-receptor antagonist (D-[S] and L-methadone)
- Presynaptic blocker of serotonin and norepinephrine re-uptake in periaqueductal gray (D-methadone)

Pharmacokinetics
- Pharmacokinetic parameter estimates in children and neonates (!) similar to those reported in adults
- Oral bioavailability: 36-100% (usually > 60-90%)
- Peak plasma concentration: 1.7-5 hr's
- Children 1-18 years (n=15): very prolonged elimination, low clearance; 19.2 [SD 13.6] [3.8-62] hours
- Onset of analgesia: 30-60 minutes
- Long half-life does NOT match the duration of analgesia (initially 4-6 hours; after repeated dosing 8-12 hours)
- No correlation between plasma concentration and dose OR analgesic effect
Renal and/or hepatic impairment does not alter clearance or dosing of methadone (possibly in severe liver disease).

Methadone: Two Compartment Model

- **High lipophilicity:**
- **Reservoir 99%:** Liver Storage, Adipose Stores, Protein binding 60-90%
- **Liver Storage:**
- **Protein binding 60-90%:**
- **Alpha-1-acid-glycoprotein = acute phase reactant [elevated in cancer]:**
- **Excretion:** urine, feces

Methadone Drug Interaction

**Inducers and Inhibitors of CYP enzymes**

- **Decreases level**
  - Carbamazepine
  - Phenytoin
  - Phenobarbital
  - Risperidone
  - Auto-induction (clearance higher once reached steady-state)

- **Increases level**
  - SSRI
  - “Azols” (e.g. fluconazole)
  - Macrolid antibiotics
  - Nifedipin
  - Tricyclic antidepressants

No grapefruit juice…?

CYP 3A4 Inhibitor
Methadone as First Line Opioid

- Methadone may be effective as first-line drug in the management of cancer pain, providing analgesia and adverse effect profiles similar to those produced by other opioids.


  - Doses tend to remain stable, suggesting that metabolic characteristics and extraopioid analgesic effects, as well as antihyperalgesic properties, may be interesting potential advantages.

  - Starting Dose (Opioid Naive): 0.05-0.1 mg/kg/dose [max 2.5 - 5 mg PO Q6-12]

  - Case reports: Low-dose Methadone 0.03-0.04 mg/kg/dose BID effective to treat refractory neuropathic pain in 2 children with cancer. Madden K, Bruera E. Very Low-Dose Methadone To Treat Refractory Neuropathic Pain in Children with Cancer. J Palliat Med. 2017;20(11):1280-1283.

Combining Opioids?

- Possible yes...

- However, more research is required.


- (...at least in mice, that is...)

Analgesic Tolerance
Low-dose Methadone & low-dose Haloperidol?

- n=43 patients; rotated to methadone 2.5 mg/day to 15 mg/day, plus scheduled haloperidol (median: 1.5 mg/day) = improved analgesia

- Sigma (σ) receptors, initially described as a subtype of opioid receptors, are now considered unique receptors

- Haloperidol antagonism of sigma-1 = antinociception in mice

- Sigma-1 Receptor antagonists remove binding to NR1 subunits of NMDA receptors, which prevents ability to restrain opioid-induced hyperalgesia

Methadone Conversion

- Opioid conversion to methadone commonly practiced; dosing was significantly lower compared to adult conversion ratios; more than 40% of children were under-medicated; majority received opioids for sedation while intubated and ventilated: therefore safe and efficacious pediatric methadone conversion rates remain unclear

- Retrospective, single-institution review of pediatric cancer patients over five years (n=41)

- Methadone (39% for neuropathic pain) was effective in treating both neuropathic and nociceptive pain that was unresponsive to other opioids
  - Starting dose 0.06-3.8 mg/kg/day [median 0.32] PO/NG (IV x3)

- 41% side effects: incl. sedation (n=10), nausea (6), constipation (6); no pruritus, no respiratory depression

Methadone Conversion- “The 30 mg Table”

- Starting Dose (Opioid Naive): 0.05-0.1 mg/kg/dose [2.5 - 5 mg PO Q6-12]

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<tr>
<td>&gt; 1000mg</td>
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</tbody>
</table>

Conversion Ratio:
Methadone Dose Ratio

- n=10 adult patients >1200 mg PO morphine equivalent: No correlation identified between high MED doses and methadone at dose stabilization after opioid rotation. [Chatham, M.S., et al. Dose ratios between high dose oral morphine or equivalents and oral methadone. J Palliat Med. 2013. 16(8): p. 947-50.]

- fixed maximum methadone dose of 30 mg/day produced clinically meaningful improvements in pain scores without adverse drug effects

Caution should be exercised before considering rotation to methadone doses higher than 30 mg/day in a patient receiving >1200 mg oral MED/day.

Conversion to Methadone From Another Opioid over 3 days

- Calculate total methadone dose. Convert step wise in order to detect if the patient demonstrates a therapeutic response to a much lower dose of methadone that you had expected. [von Gunten CF. Methadone: starting dosing information No. 86. Journal of Palliative Medicine. 2004 Apr;7(2):304-5.]

- **Day 1**: Replace 1/3 of opioid dose with oral methadone on bid or tid schedule
- **Day 2**: Replace next 1/3 of opioid dose.
- **Day 3**: Complete change to methadone.

Methadone

**Breakthrough dose...?**

- Recommendations vary


- 10% of daily dose Q2H PRN [Dorn D (2008) Motion Nased Cancer]

- Rescue dose equal or smaller BID dose Q3h PRN [Holzer D and Make J (1998) Pain Reviews. 5:51-8]


- Half the dose in half the time? e.g. 10 mg PO Q8h plus 5 mg Q4h PRN (max of 2 on 24 hrs)
Methadone

To ECG or Not to ECG... That is Still the Question....

Cardiac Toxicity of Methadone

- 1246 patients, F/U 12 months
- Rate of QTc prolongation was 49.4%.
- 2.4% had a cardiac event.
- 50.4% were at risk for an event.
- Odds ratio: age (1.06), dose > 100mg/day (6.18).

- Caution with inhibitors of CYP 2D6 and 3A4
  - SSRIs
  - "Azols" (Fluconazol etc.)
  - Macrolid antibiotics
  - Nifedipin
  - Tricyclic antidepressants
  - Grapefruit juice

- Caution should prevail - low threshold for EKG

<table>
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<tr>
<th>INITIAL OPIOID</th>
<th>BASAL / hour</th>
<th>NEW OPIOID</th>
<th>BASAL / hour</th>
<th>PCA bolus (lockout 15 min)</th>
<th>CLINICIAN ACTIVATED BOLUS</th>
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<td>5 mg</td>
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<td>5 mg</td>
</tr>
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</table>
How to Rotate from Methadone to a Different Opioid

- Quick answer
- ...don’t!

- 12/13 patients unable to complete rotation due to pain and dysphoria

- 35/39 successful conversion;
  - Methadone : oral morphine = 1:13.5 (IV); 1:4.7 (PO)

- Conversion from Methadone to other Opioid: Over 3 days reducing methadone by 1/3 per day?

- Switch to levorphanol? see
  - www.mypcnow.org/#!blank/s5bm4

Methadone Checklist

Consider Checklist!

- Inpatient vs outpatient follow up 24/7?

- Plan of action for over sedation, withdrawal, unrelieved pain?

- Documentation and handoff standardized?

- What else?

- 2 clinicians checked calculation independently?

- Prescribing provider has control over all opioids/benzodiazepines etc.?

- Everyone involved in care of patients has understood methadone guidelines!

- Vital signs are assessed and documented regularly?

Conclusions - Methadone

Methadone should not be prescribed by those unfamiliar with its use!

Its effects should be closely monitored for several days, particularly when it is first started and after any dose changes.

Opioid rotation: Maximum starting dose of methadone usually not above 30 mg PO / day
Pediatric Multimodal Analgesia

**Basic Analgesics**
- Acetaminophen (Paracetamol)
- NSAIDs / COX-2 Inhibitor

**Opioids**
- Tramadol ("weak")
- Morphine ("strong")
- Fentanyl, Hydromorphone, Oxycodone, Methadone (UK: Diamorphine)

**4 WHO Principles**
- "By the Clock"

**Integrative Therapies**
- Mind-Body Techniques
  - Hypnosis, Biofeedback, Abdominal Breathing, Progressive Muscle Relaxation, Mindfulness, Distraction
- Acupressure, Acupuncture
- Aromatherapy, Massage

**Integrative Pain Management**

**Integrative modalities**
- **Integrative modalities effective in management of pediatric pain**
  - Hypnosis
  - Guided imagery
  - Yoga
  - Acupuncture
  - Massage
  - Biofeedback

**References**
- Dobson, C.E.; Byrne, M.W. Original research: Using guided imagery to manage pain in young children with sickle cell disease. The American journal of nursing 2014, 114, 26-36; test 37, 47.
How does this stuff work...?


- Distraction significantly increased activation of cingulo-frontal cortex including orbitofrontal & perigenual anterior cingulate cortex (ACC), as well as periaqueductal gray (PAG) & the posterior thalamus.


Words are, in my not-so-humble opinion, our most inexhaustible source of **magic**. Capable of both inflicting injury, and remedying it

Prof. Albus Dumbledore

Do You Want to Go to Your Favorite Place?
Breathing

Acupuncture / Acupressure
Aromatherapy / Essential Oils

- **Lavender** (Lavandula angustifolia)
- **Lemon** (Citrus limon)
- **Peppermint** (Mentha piperita)
- **Spearmint** (Mentha spicata)
- **Sweet orange** (sweet orange)

### Table

<table>
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<th></th>
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Magic…?

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**Multimodal (Opioid-sparing) Analgesia**

- **Basic Analgesics**
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- **WHO Principles** (not specified)

- **Integrative Therapies**
  - Mind-Body Techniques (Hypnosis, Biofeedback, Abdominal Breathing, Progressive Muscle Relaxation, Mindfulness, Distraction)
  - Acupressure, Acupuncture
  - Aromatherapy, Massage

- **Rehabilitation**
  - Exercise
  - Physical Therapy
  - Graded motor imagery, mirror therapy
  - Occupational Therapy, Speech Therapy

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Friedrichsdorf SJ: 12th Pediatric Pain Master Class in Minneapolis, MN, June 13-19, 2020
Graded Motor Imagery

- Process of thinking about moving without actually moving.
- Cortical reorganization and associated changes in somatosensory cortex activity and anatomy in certain types of chronic pain (e.g., CRPS; lower back pain).
- Degree of cortical reorganization correlated with pain intensity.

Mirror Therapy for Phantom Limb Pain in a 7-Year-Old Male with Osteosarcoma

Pediatric Multimodal Analgesia

Basic Analgesics
- Acetaminophen (Paracetamol)
- NSAIDs / COX-2 Inhibitor

Psychology
- CBT: Cognitive Behavioral Therapy, Skill-Based Training

Integrative Therapies
- Acupuncture, Acupressure
- Aromatherapy, Massage

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- Exercise
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- Occupational Therapy

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- Tramadol (“weak”)
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WHO Principles
- “By the Clock”

Multimodal (Opioid-sparing) Analgesia

Pediatric Multimodal Analgesia

Psychology Intervention

- Postoperative Pain - Systematic Review
- Psychological Treatments significantly reduce pain intensity reported by children and adolescents with headache, abdominal pain, and fibromyalgia.
- Psychological Treatments significantly reduce pain intensity reported by children and adolescents with headache, abdominal pain, and fibromyalgia.

Psychological Treatments effective in reducing children’s self-reported pain: distraction/imagery interventions effective.

- Affective, anxiety, & behavior disorders early risk factors of chronic pain (rather than vice versa).
Pediatric Multimodal Analgesia

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Psychology
- CBT (Cognitive Behavioral Therapy), Behavioral Training

Integrative Therapies
- Mind-Body Techniques (Hypnosis, Biofeedback, Abdominal Breathing, Progressive Muscle Relaxation, Mindfulness, Distraction)
- Acupressure, Acupuncture, Aromatherapy, Massage

Regional Anesthesia
- Neuraxial infusion
- Peripherally Inserted Port / Pump, Neurolytic block

Rehabilitation
- Exercise, Physical Therapy, Occupational Therapy, Speech Therapy

Adjuvants
- Alpha-Agonist: Clonidine, Dexmedetomidine
- Gabapentinoids
- TCA's: Amitriptyline, Nortriptyline
- NMDA-Antagonists: Ketamine
- Na-channel blocker: Lidocaine

Multimodal (Opioid-sparing) Analgesia

Regional anesthesia approaches to pain management in PC

- Regional anesthesia: pediatric knowledge limited to case reports and case series
  - central neuraxial infusions
  - peripheral nerve and plexus blocks or infusions
  - neurolytic blocks
  - implanted intrathecal ports & pumps for baclofen, opioids, local anesthetics, and other adjuvants
- Neurolitic Sympathectomy
  - RCT (n=109) inoperable abdominal or pelvic cancer: better pain control, less opioid consumption, and better quality of life

Multimodal (Opioid-sparing) Analgesia

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- Neurolitic Sympathectomy
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Do you remember Marius...?

How about a Plan B?

LET Anesthesia

- Sitting upright
- Distraction
- Topical Anesthesia

- 3mL LET gel: Lidocaine 4% - Epinephrine 0.18% - Tetracaine 0.5%


If adequate procedural analgesia not feasible with the “4 Non-Negotiables” alone, refer patient to:

1. Child Life (shouldn’t have been involved by now?)
2. Needle Phobia: psychology (CBT)
3. Mild sedation: Nitrous gas


4. Moderate/deep sedation (e.g. ketamine, propofol)

Note:
A sedative alone (such as a benzodiazepine) can *never* be a substitute for procedural analgesia.

What’s Plan B?

If adequate procedural analgesia not feasible with the “4 Non-Negotiables” alone, refer patient to:

1. Child Life (shouldn’t have been involved by now?)
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Note:
A sedative alone (such as a benzodiazepine) can *never* be a substitute for procedural analgesia.
IV Access Under Nitrous Gas

22 months-old, Lidocaine 4% cream in place, needed IV for radiologic procedure, history of challenging IV access in the past.

Thanks to Patricia D. Scherrer MD
Children’s Hospitals and Clinics of Minnesota

12-year-old Boy with metastatic neuroblastoma with increasing nociceptive (VAS 7/10) and neuropathic (VAS 9/10) pain; no over sedation

Current Opioids
- Fentanyl Patches: 2 x 100 mcg/hr Q72h
- Oxycodone ER: 30 mg BID PO
- Oxycodone: 5mg tablets x7 day
- Morphine: 10 mg x 12/ day PO

Methadone Conversion- “The 30 mg Table”
... actually 60mg ... reduced by 50% for incomplete cross tolerance

* Starting Dose (Opioid Naive): 0.05-0.1 mg/kg/dose [2.5 - 5 mg PO Q6-12]

Conversion Ratio:

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**Jake: Total Opioid Use in IV Morphine Equivalent**

- **Fentanyl Patches**: 2 x 100mcg/hr Q72h

- **Oxycodone ER**: 30 mg BID PO
  - = 60 mg/day

- **Oxycodone (5mg)**: 7 tablets/day

- **Morphine**: 10 mg tablets x 12/day

**IV Morphine/24h**

<table>
<thead>
<tr>
<th>IV Morphine</th>
<th>Total: mg</th>
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**Intravenous Morphine**

- IV Morphine
- IV Morphine
Methadone Conversion - “The 30 mg Table”

- Starting Dose (Opioid Naïve): 0.05-0.1 mg/kg/dose [2.5 - 5 mg PO Q6-12]

Conversion Ratio:

<table>
<thead>
<tr>
<th>Total Daily Oral Morphine Dose</th>
<th>Estimated Daily Oral Methadone Requirement</th>
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</thead>
<tbody>
<tr>
<td>&lt; 100 mg</td>
<td>3:1  20% - 30%</td>
</tr>
<tr>
<td>101 mg - 300mg</td>
<td>5:1  10% - 20%</td>
</tr>
<tr>
<td>301 mg - 600mg</td>
<td>10:1  8% - 12%</td>
</tr>
<tr>
<td>601 mg - 800mg</td>
<td>12:1  5% - 10%</td>
</tr>
<tr>
<td>801 mg - 1000mg</td>
<td>65 mg  39 - 78 mg</td>
</tr>
<tr>
<td>&gt; 1000 mg</td>
<td>10:1  8% - 12%</td>
</tr>
</tbody>
</table>

Jake [PO Methadone]

- He had excellent pain control for 4 weeks on Methadone 12 mg PO Q8h (6mg PRN once every 2 days) - unfortunately, he develops a bowel obstruction and is unable to swallow medication

Jake [PO Methadone]
Jake would like to thank you for your excellent opioid analgesia management.

So, how do we treat the individual pain patient in front of us?

Crystal clear answer:
So, how do we treat the individual pain patient in front of us?

“**It Depends**”
-Socrates

Pain
- Psychological pain
- Chronic Pain
- Mental Health
- Anxiety
- Nociceptive Pain
- Depression
- Neuropathic Pain
- School absenteeism
- Social Pain
- Poor sleep hygiene
- Visceral Pain
- Delirium
- Total Pain
- Withdrawal

Racial Disparity

Poor sleep hygiene

Spiritual Pain

School absenteeism

Visceral Pain

Delirium

Total Pain

Withdrawal

Mental Health

School absenteeism

Visceral Pain

Delirium

Total Pain

Withdrawal
Conclusions

- **Prevent needle pain for every child every time:**
  Apply topical anesthesia - and do NOT hold them down

- **Use multimodal analgesia:**
  Multiple agents, interventions, rehabilitation, psychological and integrative therapies act synergistically for more effective pediatric pain control with fewer side effects than single analgesic or modality

- **Methadone** is an excellent analgesic AND not be prescribed by those unfamiliar with its use!
  Its effects should be closely monitored for several days, particularly when it is first started and after any dose changes.

- **Opioid rotation:** Maximum starting dose of methadone usually not above 30 mg PO /