The Illusion of Opioids

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Common quote:

“Opioids are the most potent medications we have for treatment of pain.”


Opioid facts

The United States has 4.6% of the world’s population.

• We use most of the world’s opioids.¹

• 83% of the world’s population has no access to any opioids.²

Opioid increase

Drug distribution through the pharmaceutical supply chain was the equivalent of 96 mg of morphine per person in 1997.

and approximately 640 mg per person in 2015, an increase of >500%.⁴,⁴⁸

That is the equivalent of 128 Vicodin tablets!

Disclosure

Neither I nor any members of my immediate family have a financial interest/arrangement or affiliation that could be perceived as a real or apparent conflict of interest related to the content or supporters of this activity.
From 2016 to 2017, overdose deaths increased by 171. An increase of 17%.

U.S. life expectancy decreased for the first time in decades. U.S. mortality rate increased. All driven by opioid overdoses!

Opioid overdoses counteracted all other medical advances!

Three key concepts:

Prescribers:
1. Don’t understand pain.
2. Don’t understand opioids.
3. Don’t understand addiction.

PAIN
**Pain**

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

International Association for the Study of Pain

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**Pain**

Acute pain: Pain < 3 months  
Chronic pain: Pain > 3 months  
Acute pain is a *symptom*  
Chronic pain is a *disease*

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**4 types of pain**

- Nociceptive
- Neuropathic
- Central Sensitization
- Opioid withdrawal

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**The Pain Pathway**

- Site of injury
- Brainstem
- Spinal cord
- Nociceptors
- Pain fibers
- Sensory neurons
- Motor neurons
- Spinal cord synapses
- Thalamus
- Pain processing

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**Which square is darker... A or B?**

- Constancy
Better keep an eye on them...
Better keep an eye on them...

Pretty cool, huh?

“Lightness Constancy”

Pain pathways

Nociceptor
Spinothalamic nerve
Thalamus

Amygdala (fear)
Hippocampus (memory)
Somatosensory nerve (pain)
Limbic system (emotion)
Prefrontal cortex (rational thinking)

Central sensitization

Nociceptor
Spinothalamic nerve
Thalamus

Amygdala (fear)
Hippocampus (memory)
Somatosensory nerve (pain)
Limbic system (emotion)
Prefrontal cortex (rational thinking)

Central Sensitization Syndromes

• Fibromyalgia
• Chronic headaches
• Irritable bowel syndrome
• Chronic neck pain
• Chronic back pain
• Interstitial cystitis
• All chronic pain???

Central sensitization Inventory

Subclinical = 0 - 29
Mild = 30 - 39
Moderate = 40 - 49
Severe = 50 - 59
Extreme = 60 - 100.
Radiofrequency denervation

- Over 600 patients with CLBP and no improvement with conservative measures.
- 50% received denervation. All had a standardized exercise program.
- No difference in pain at 3 months.

Opioid withdrawal pain

- Occurs with reduction in opioid dose for those who have been on opioid therapy – even for acute pain treatment.
- Usually felt in the area where there is a history of pain.

Acute to chronic back pain

<table>
<thead>
<tr>
<th>Patient-specific factors</th>
<th>Treatment factors</th>
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</thead>
<tbody>
<tr>
<td>1 Anxiety and/or depression</td>
<td>Prescribing of opioids for acute pain*</td>
</tr>
<tr>
<td>prior to injury</td>
<td></td>
</tr>
<tr>
<td>2 Home and/or work environment</td>
<td></td>
</tr>
<tr>
<td>3 Activity level prior to injury</td>
<td></td>
</tr>
<tr>
<td>4 Severity of injury</td>
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</table>

*This does not apply to severe trauma when opioids should be used briefly.

Optimism and pain

A 2019 study showed that soldiers having low optimism had a 35% greater chance of developing pain after deployment than soldiers with high optimism.

Chronic pain causes

- Nociceptive
- Neuropathic
- Central Sensitization
- Opioid withdrawal
- Combination (this is most common)

Central Sensitization is a significant factor in most cases of chronic pain that cause people to see the doctor.
All addictive substances stimulate dopamine

- Opioids
- Alcohol
- THC
- Cocaine
- Methamphetamine
- Nicotine
- LSD
- Ecstasy
- Behaviors also...

Opioids are different...

Dopamine +
Opioid receptors

Opioid receptors and endorphins

What is the purpose of our endorphins?
Enable us to achieve a goal (short term).23,24
- Decrease pain (minimal effect).
- Increase motivation.
- Increase confidence.
- Increase reward.
- Reduce depression and anxiety.
- Increase “warmth-liking”.25
- Liking warm things.
- Interpersonal bonding. “A hug from God!”

Primary purpose:

Dopamine – Our primary reward system. This is what we live for.

Endorphins and opioid receptors – These maximize our ability to achieve the reward. This is our “success system”!
The “Dorothy Reaction”

- Occurs in susceptible individuals on exposure to opioids:
  - Those with acute or chronic stress/anxiety
  - Those with depression
  - Those with high ACE scores
  - Those with a genetic predisposition
  - Those with substance use disorder (including smoking)
  - Others...

Opioids given for pain may cause the “Dorothy Reaction and:

- Mentally impairing
- Delay recovery
- Increase medical costs
- Opioid hyperalgesia
- Double the chance of disability (if prescribed for 7 days or more)
- Increase falls
- Cardiac
- GI
- Treat depression (They are very calming)
- Brain changes
- Addiction

Opioids and Central Sensitization

- Opioids should probably never be used when there is a significant component of central sensitization!
- Opioids initially relieve the depression and anxiety that drive pain in CS but with ongoing use make these worse and therefore make pain worse.

Addiction

Acute rx leads to long-term use

Duration of acute use:
- 1 day - 6% chance of still using that drug a year later.
- 8 days - 13.5%.
- 31 days - 29.9%.
Teens who received a prescription for opioid pain medication by Grade 12 were at 33 percent increased risk of misusing an opioid between ages 19 and 25. Among those with low predicted risk of future opioid use in 12th grade, having an opioid prescription increased their risk of post-high-school opioid misuse threefold.

Adolescents and young adults who received a dental opioid rx

A review of adolescents and young adults (ages 16-25) who were insured in 2015 found that:
- 12.9% received one or more prescriptions for an opioid.
- Of those, 30.6% got that rx from a dentist.

Adolescents and young adults who received a dental opioid rx

Of those that got an rx from a dentist, 6.9% received another opioid rx 3-12 months later.
Only 0.1% of controls who did not get an opioid got an rx 3-12 months later.
5.8% of those that received an opioid had a health encounter with an opioid abuse related dx in the next year c/w 0.4% of those who did not get an opioid.43

The “Gray Area”

Chronic pain on opioids vs Opioid Use disorder with pain

Treating Pain

It is important that we keep opioid naïve people opioid naive!
Efficacy of pain medications
Acute pain

<table>
<thead>
<tr>
<th>Pain Mediation</th>
<th>Percent with 50% pain relief</th>
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<tr>
<td>Ibuprofen 200 mg</td>
<td>37</td>
</tr>
<tr>
<td>Acetaminophen 500 mg</td>
<td>28</td>
</tr>
<tr>
<td>Ibuprofen 400 mg</td>
<td>49</td>
</tr>
<tr>
<td>Diphenhydramine 15 mg</td>
<td>21</td>
</tr>
<tr>
<td>Cyo 12 x acet 500 mg</td>
<td>37</td>
</tr>
<tr>
<td>Ibu 200 x acet 1000 mg</td>
<td>60</td>
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Post-op pain

- Enhanced recovery after surgery (ERAS)
- 109 patients having colorectal surgery c/w 98 controls
- Protocol includes:
  - Pre-op counseling
  - Carbohydrate loading
  - Multimodal analgesia with avoidance of intravenous opioids
  - Intraoperative goal-directed fluid resuscitation
  - Immediate postoperative feeding
  - Immediate ambulation

ERAS outcomes

ERAS patients compared to controls:
- Ambulated on POD 0: 77% (0%)
- Total morphine equivalents: 63 (280)
- Any complication: 15% (30%)
- Length of stay in days: 4.6 (6.8)
- Hospital costs: $13,306 ($20,435)
- Press-Ganey patient satisfaction: 98% (43%)

Renal colic

Delivering safe and effective analgesia for management of renal colic in the emergency department: a double-blind, multigroup, randomised controlled trial

Acute pain conclusion:

We must prescribe fewer opioids for acute pain!
The CDC guidelines recommend 3 days or less – but most outpatient pain can be treated without any opioids!

The combination of ibuprofen + acetaminophen is the best treatment with the least side effects.
If you use opioids for acute pain:

- They are most helpful for their calming effects.
- Use for 3 days or less.
- Check KASPER first!

**Chronic pain**

- Completely different from acute pain!
- If the pain is severe or disabling, **most** is from central sensitization and/or opioid withdrawal.
- Pain medications will not work well on this type of pain.

**Chronic pain and opioids**

No evidence that opioids are effective for long-term treatment of chronic pain.²⁰

Epidemiologic studies have shown that those on chronic opioid therapy have worse quality of life than those with chronic pain who are not.²¹

The AAN recommends against using opioids for back pain, headaches, or fibromyalgia.²⁷

A Cochrane review recommends against using opioids for OA of the hip or knee.²⁶

**Opioid efficacy for chronic back pain**²⁵

- Short term studies (<3 mo) pain decrease 10.1 (100 pt scale)
- Medium term studies (3 mo - <6 mo) pain decrease 8.1
- Long term (6 mo or more) — NO STUDIES

Experts believe that there must be a decrease of 15 points to be clinically significant.

**Opioids and Central Sensitization**

- Opioids should probably never be used when there is a significant component of central sensitization!
- Opioids initially relieve the depression and anxiety that drive pain in CS but with ongoing use make these worse and therefore make pain worse.

**Treatment of chronic pain**

- **Behavioral therapy**²²
- PT, OT, ST
- Treatment of mood disorders
- Exercise
- Acupuncture
- Yoga and other alternative therapies
- Amitriptyline, duloxetine, gabapentin and similar drugs may help a little.
Treatment of chronic pain

- Behavioral therapy:
  - Cognitive Behavioral Therapy
  - Redirect your thoughts
  - Mindfulness training
  - Acknowledge your thoughts without judgement
  - Decatastrophizing

There is very limited availability of this type of therapy.

Additional thoughts:

- If your patient on opioids is not doing functionally better, you should wean them off.
- If you believe your patient has developed opioid use disorder, you must treat them or refer them for treatment. MAT is the most effective treatment of OUD.

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 expected benefits do not outweigh risks to the patient, clinicians should avoid prescribing opioids, including extended-release or long-acting opioid formulations, for chronic pain.

2. Before starting opioid therapy for chronic pain, clinicians should evaluate whether the patient has a history of opioid use disorder, even if the condition is in remission. Patients with a history of opioid use disorder are more likely to misuse or abuse prescribed opioids, to develop a tolerance to opioids, to require higher doses of opioids, and to experience adverse events such as overdose, addiction, and withdrawal.

3. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function and if the ongoing risks to the patient are outweighed by the benefits. Clinicians should consider offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥90 morphine milligram equivalents [MME]/day or ≥50 MME/day), or concurrent benzodiazepine use, are present.

4. Clinicians should address patient concerns and challenges as they arise, including offering naloxone when factors that increase risk for opioid overdose are present.

5. Clinicians should review patient history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose are present.

6. For acute pain. Use opioids for 3 days or less.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should continue opioid therapy only if the ongoing risks to the patient are outweighed by the benefits. Clinicians should consider offering naloxone when factors that increase risk for opioid overdose are present.

9. Clinicians should review the patient’s history of controlled substance prescriptions using state PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies).
For patients already on opioids for COT

- Check the PDMP regularly
- Do not co-prescribe benzodiazepines or carisoprodol
- You should wean off if no significant functional improvement
- Think carefully before increasing the dose
- Co-prescribe naloxone
- Don’t use methadone
- Consider a change to buprenorphine (transdermal, buccal, or SL) (This is not in the CDC Guideline)

Weaning is hard!

Darnall Pain Study 2018

| Change in Opioid Morphine Equivalent Daily Dose and Absolute Change in Pain Intensity Score From Baseline to Month 4 for Study Completers. NRS indicates numeric rating scale. |
|-------------|------------------|----------------|------------------|------------------|------------------|------------------|------------------|
| Change in Pain Score | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 |
| Change in Opioid Dose | -100 | -50 | 0 | 50 | 100 | Increase | Decrease |

<table>
<thead>
<tr>
<th>Study details</th>
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<tbody>
<tr>
<td>Patients in an outpatient pain clinic.</td>
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<tr>
<td>Given a booklet on pain and taper suggestions.</td>
</tr>
<tr>
<td>110 eligible for taper</td>
</tr>
<tr>
<td>82 agreed to taper (75%)</td>
</tr>
<tr>
<td>51 (of 82) completed 4 months and final survey</td>
</tr>
<tr>
<td>Mean MED decreased from 288 to 150</td>
</tr>
<tr>
<td>About 90% were able to decrease their dose</td>
</tr>
<tr>
<td>86% had no change or a decrease in their pain</td>
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</tbody>
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Tapering opioids – 2 other studies

Opioid taper in people on COT resulted in average pain decrease from 7.1 to 5.4. A 24% decrease in pain. About 1/3 of patients ended up going back on opioids but their pain was not improved on the opioids.34
Taper off of COT reduces pain in all ages. Approximate 20% reduction. Also reduction in depression and pain catastrophizing.35
When are opioids definitely indicated?

- Following severe trauma (for a short period)
- End of life

OUD Treatment

Treatment of Opioid Use Disorder

Detox and abstinence: Success rate ≈ 10%
Methadone: Success rate ≈ 60%
Buprenorphine (Suboxone®): Success rate ≈ 50%
Naltrexone injection (Vivitrol®): Success rate ≈ 10%

Residential treatment?

Residential treatment of opioid use disorder without medications (detox and abstinence treatment only) increases the risk of death.65

137 people admitted to a 28-day detox and residential treatment program:
- 43 left prior to finishing detox – none died.
- 54 completed detox but left prior to completing 28 days – 1 died.
- 37 completed detox and 28 day program – 4 died.
Naltrexone – real world

Why I love treating Opioid Use Disorder...

You help people go from the worst point in their life to the best!

It is really easy (for the provider).

It is very safe.

You get way more credit than you deserve!

It is important that we keep opioid naïve people opioid naïve!

“To write prescriptions is easy, but to come to an understanding with people is hard.”

-- Franz Kafka, “A Country Doctor”

References:


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