Opioid Addiction Treatment ECHO

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Introduction to Opioid Use Disorder

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https://www.amazon.com/Model-Neuroscience-Based-Blueprint-Integrated-Addiction/dp/1498773052
Disclosures

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Dr. Chambers
  *Enfoglobe : Medical data analytics and education software
  *Indigobio : Biological Fluids testing and data analytics.
  *Proniras: Biotech start up/CNS active orphan drug development
What are opioids?

“Opioid” refers to endogenous, natural and synthetic members of this drug class:
Quite broad, generally any molecule active at brain opioid receptors
Opiates: natural and synthetics.

“Natural”, referred to as “opiates”

• Derived from opium poppy
• Morphine, codeine, opium

Synthetic (partly or completely):

• Semisynthetic: heroin, hydrocodone, oxycodone
• Fully Synthetic: fentanyl, tramadol, methadone
Opioids

Use of opiates for *acute* pain is one of the major miracles of modern medicine.

Heroin $50-200 \text{ K/kg}$  
30-70% pure

Oxycontin:

<table>
<thead>
<tr>
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<th>Rx</th>
<th>Street</th>
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<tbody>
<tr>
<td>10 mg</td>
<td>$1.25</td>
<td>$5-20</td>
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<tr>
<td>80 mg</td>
<td>$6.00</td>
<td>$65++</td>
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methadone  
fentanyl  
heroin  
oxycodone  
hydrocodone  
Buprenorphine  
tramadol
Opioid Intoxication

- Drowsy, sedated ("nodding")
- Speech and movement may be slowed
- May appear confused or incoherent
- May appear euphoric ("high")
- Pupils are constricted ("pinpoint")

General Effects

- Addiction
- Pain relief (analgesia)
- Cough suppression
- Constipation
- Sedation (sleepiness)
- Respiratory suppression (slowed breathing)
- Respiratory arrest (stopping breathing)
- Death

Opioid Withdrawal
Generally opposite of the above: Cold Turkey, increase Vitals, tremor
Sweating, crying, nasal discharge, agitation, dysphoria
Endorphins
(18+)
Prodynorphin
Proenkephalin
Proopimelanocortin

Also kappa and delta opiate receptors

\[ \text{striatum} \begin{cases} 
\text{Dynorphins} & \text{enkephalins} \\
(\text{Substance P}) & 
\end{cases} \]

MU RECEPTOR is primary Receptor active in analgesia, Addiction, Euphoria and CNS/respiratory depression

G protein mechanism…mu’s inhibit Adenylate cyclase and activate K+ channels (out of the cell)

Image from Neuropsychiatry, Fogel, Shiffer & Rao, 1993
Acute DA discharge has intracellular effects in the NAc

Inside a NAc neuron
What does cAMP/PKA do in the Cell?

Cytoplasm

Nucleus
What does this mean for Neuronal Form and Function?

Li, Acerbo, and Robinson, 2004 Europ J Neurosci
Neuronal changes due to chronic morphine administration

Robinson et al. (2002) Synapse
DSM-V: Substance Use Disorder (Addiction)

Problematic pattern of use causing clinically significant impairment or distress within a year including 2 or more of:

1. Escalation in amounts of drug or time spent using
2. Persistent Desire to quit and/or failed attempts to quit
3. Great time spent acquiring or recovering from the substance
4. Escalation of significant craving and desire to use
5. Recurrent use causes occupational, educational, and family role failures
6. Recurrent use disrupts relationships
7. Recurrent use reduces or eliminates social, occupational, or recreational activities
8. Recurrent use creates physical danger
9. Recurrent use persists despite knowledge that use is causing physical or mental health problems
10. Tolerance
11. Withdrawal

Nicotine, alcohol, cannabis, cocaine, amphetamine, opiates (2-3 Mild, 4-5 Moderate, 6+ Severe)
Why Have Opioids Become Such a Big Problem in the US?

• 1990s: New norm that all pain should be eliminated
  • pain as the “5th vital sign”

• Pharmaceutical company promotion

• Opioid over-prescribing

• Diversion, and widespread non-medical use of opioids, especially among youth

• Heroin widely available and less costly

• Limited access to medication treatment
The Iatrogenic Opioid Addiction Epidemic

- In 2010, narcotics were prescribed in the U.S. at levels equivalent to medicating every single adult with a 5 mg hydrocodone 6 x/day for a month.

- By 2008, an American adult is as likely to die from a prescription opioid overdose than either suicide or a motor vehicle accident.

CDC, MMWR, 60:43 2011
Unintentional Drug Overdose Deaths
United States, 1970-2007

In 2007, there were 9.18 deaths per 100,000 population due to unintentional drug overdose, based on 27,658 deaths.

Source: Centers for Disease Control and Prevention. Unintentional Drug Poisoning in the United States (July 2010).
“Pseudoaddiction”

“iatrogenic syndrome that mimics the behavioral symptoms of addiction” … in patients receiving inadequate doses of opioids for pain. A syndrome caused by doctors withholding opioids (due to fear of causing addiction) that must be treated with more and higher doses of opioids. —(Weissman and Haddox, 1989)

‘Pseudoaddiction’ proliferated and was accepted widely in the medical literature, penetrating medical dictionaries, textbooks, and being the subject of at least 224 peer-review publications. About 10% of this literature listed funding sponsorship by pharmaceutical companies (e.g. Purdue Pharma) that are the industry leaders in the manufacturing and sale of prescription opioids (oxycodone, meperidine, morphine, hydromorphone, oxymorphone, tramadol, etc.) - (Greene & Chambers, 2015, Curr Addiction Reports)
“Follow the Money.”

‘Deep throat’ to Bob Woodward
-- In “All the President’s Men” (1976)

PAIN As 5th Vital Sign, VA+ JAACHO Pain Initiative
Sponsored by Purdue Pharm and other companies
Age-Adjusted Overdose Death Rates Related to Prescription Opioids and Heroin in the United States, 2000–2014
What Can Primary Care Teams do to Address Opioid Use Disorder?

• **Prevention**: Responsible opioid prescribing (CDC Guideline 2016)
  - Includes 3 main principles:
    - Use non-opioid therapies:
      - Use non-pharmacologic therapies and non-opioid pharmacologic therapies
      - Establish and measure goals for pain and function
      - Don’t routinely use opioids to treat chronic pain
    - Start low and go slow:
      - Start with lowest possible effective dose
      - Start with immediate release, rather than long-acting
      - Only prescribe amount needed for expected duration of pain
      - Taper and discontinue if no improvement or risks of harms outweigh benefits
    - Close follow-up:
      - Check prescription monitoring program and urine drug tests
      - Avoid concurrent benzos and opioids
      - Arrange treatment for opioid use disorder if needed
What Can Primary Care Teams do Besides Prevention to Address Opioid Use Disorder?

• Screening: detection and early intervention for risky use
• Prevent diversion: close monitoring of patients on opioids, use of prescription monitoring programs and urine drug screens
• Harm reduction: overdose prevention, infection prevention through syringe exchange and vaccination
• Treatment: **Medication treatment** for Opioid Use Disorder is highly effective in reducing relapse, overdose, and other harms. Behavioral treatments and peer support also help to prevent relapse.
• Address co-occurring medical, psychological, and social barriers to health
References


Botticelli MA, Koh HK. Changing the language of addiction. JAMA October 4, 2016;316(13):1361


CDC Opioid Overdose Information
https://www.cdc.gov/drugoverdose/epidemic/


