Opioid Addiction: Understanding a Global Epidemic

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"At this point, we know it's addictive."
What is Addiction?

 Addict (verb) - “to devote or give (oneself) habitually or compulsively”; from Latin addicere - bound to or enslaved

 Core Components of Addiction
   Continued Behavior Despite Adverse Consequences
   Diminished or Lost Control / Compulsive Engagement
   Craving or Urge State Component
Motivational Neural Circuits

- Multiple brain structures underlying motivated behaviors.

- Motivated behavior involves integrating information regarding internal state (e.g., hunger, sexual desire, pain), environmental factors (e.g., resource or reproductive opportunities, the presence of danger), and personal experiences (e.g., recollections of events deemed similar in nature).
Role of Dopamine

- Dopamine release into the nucleus accumbens - translates motivated drive into action - a “go” signal

- Dopamine release associated with rewards and reinforcing

- Dopamine release - maximal when reward is most uncertain, it plays a central role in guiding behavior during risk-taking situations.
The endogenous opioid system influences the experiencing of pleasure.

Opioids modulate mesolimbic dopamine pathways via disinhibition of GABA input in the ventral tegmental area.
Opioid Use Disorder

A problematic pattern of opioid use leading to clinically significant impairment or distress (manifested by at least 2 of the following within a 12-month period):

1. Opioids are often taken in larger amounts or over a longer period than was intended.

2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.

3. A great deal of time is spent in activities necessary to obtain opioids, use them, or recover from its effects.

4. Craving, or a strong desire or urge to use opioids.
5. Recurrent use resulting in a failure to fulfill major role obligations.

6. Continued use despite having persistent or recurrent social or interpersonal problems

7. Important social, occupational, or recreational activities are given up or reduced because of use.

8. Recurrent use in situations in which it is physically hazardous.

9. Use continued despite knowledge of having a persistent or recurrent physical or psychological problem.

10. Tolerance

11. Withdrawal
What Are Opioids?

- Opioids are natural or synthetic substances that act on the brain’s opiate receptors.
- Opioids dull pain and relieve anxiety that comes from thinking about pain.
- People abuse opioids because they provide a feeling of euphoria (a “rush”).
Opium History

- Between 400 -1200 AD Arab traders introduced opium to China.
- 14th century Ottoman Empire-opium used to treat headache and back pain.
- 15th century China- first officially recorded use of opium as a recreational drug.
- 1874- heroin developed
- 1898- heroin marketed by Bayer as safe pediatric cough suppressant
Heroin

- **1874**-first synthesized by an English chemist
  - Diacetyl-morphine
- **1897**-resynthesized by Felix Hoffman working for Bayer trying to produce codeine
- **1898-1910**-marketed as a cough suppressant and non-addictive morphine substitute
  - Then discovered it was metabolized to morphine
- **1914** Harrison Narcotics Act banned sale and distribution
- **1924** became a Schedule 1 drug
Opiates & Opioids

**Opiates** = naturally present in opium
- e.g. morphine, codeine, thebaine

**Opioids** = manufactured
- Semisynthetics are derived from an opiate
  - heroin from morphine
  - buprenorphine from thebaine
- Synthetics are completely man-made to work like opiates
  - methadone
How did we get here?

1990s

- Under-treatment of pain
- Early data that opioid risks were low, some of which intentionally minimized
- Ease of medications for treatment
Epidemiology of Addictions
Epidemiology

Prescription opioids
- National Survey on Drug Use and Health
  - > 12 million reported non-medical use of prescription opioids
  - Estimated 1.6 million met criteria for prescription opioid abuse or dependence

Heroin
- National Household Survey on Drug Abuse
  - > 500,000 reported past year heroin use
  - Approximately 323,000 individuals met criteria for heroin abuse or dependence

Combined, 2 million opioid dependent in U.S.
Death rates from overdoses of heroin or prescription opioid pain relievers (OPRs), by age group

Chronic Pain

Pain lasting most of the day during most days for > 3 months

Point prevalence in U.S. adults: 15-20%

Lifetime prevalence in U.S. adults: 50-75%

Pain is most often-reported symptom in office visits after upper respiratory infections

Multi-faceted disorder that, by definition, is bio-psycho-social
Developmental Biology

- Addiction generally starts in young adulthood.

- Environmental and genetic influences - vulnerability to and expression of addictive disorders

- Changes in brain structure and function during adolescence might influence the motivation to engage in risk-taking behaviors.
Brain Development

- During late childhood, neurons increase their number of connections.

- But around **11 – GIRLS; 12½ - BOYS:**
  - Some of these connections are pruned off.
Notice: Judgment is last to develop!
Age 24

Balance

Judgment

Emotion

Motivation

Physical coordination, sensory processing
Youth Problem Behaviors

- delinquency
- sexual behavior
- opioids
- smoking
- drug use
- male
Opioid Withdrawal Symptoms

- Pupillary dilation
- Watery eyes
- Runny nose
- Muscle spasms ("kicking")
- Yawning, sweating, chills, gooseflesh
- Stomach cramps, diarrhea, vomiting
- Restlessness, anxiety, irritability

Usually result in further use to quiet symptoms
Changes in Neurobiology

Repeated exposure to short acting opioids leads to neuronal adaptations

- Mesolimbic dopaminergic system
- adaptations in G protein-coupled receptors
- changes in transcription and translation

Adaptations

- Mediate tolerance, withdrawal, craving, self-administration
- Provide insight into the chronic and relapsing nature of opioid dependence
Consequences

Drug-seeking Behavior → requests for opioid medications for the purpose of getting high

Aberrant Behaviors → among patients on opioids for chronic pain, behaviors that may be indicative of misuse or addiction
- Early refills
- Frequent phone calls
- Doctor shopping
- Prescription forgery
Consequences

- HIV
- Hep C
- Infections
- Overdose
- Death
Treatment
**Antecedent (Triggers)**

- Particular people
- Environment
- Feelings
e.g., urges, argument with spouse, boredom, anxiety

**Thoughts/Feelings**

**Behavior**

- Alternate behavior
e.g., I drove by the bar, next think I knew it was last call
- Abstinence
e.g., I thought about the effect it would have on my family, and took a different route home

**Consequence**

- Positive
e.g., I used and I forgot about that argument with my wife
- Negative
e.g., the next day, I felt like I’m a failure.
Contingency Management

- Re-arranging the reinforcers in a person’s environment
- Incentives or rewards to encourage specific behaviors
  - Vouchers, prizes, group acknowledgements, take-home dosing privileges, family privileges
Pharmacologic Treatment

Pharmacologic withdrawal - “detoxification”

Opioid antagonist treatment

- Naltrexone

Opioid agonist/partial agonist treatment

- Methadone
- Buprenorphine
Methadone

- Federally licensed facility
- Daily observed dosing
- Authoritative review of 11 randomized clinical trials with 1,969 patients

Conclusion methadone is superior to placebo in:
  Retaining patients in treatment
  Reducing illicit opioid use
Advantages of Methadone

- 70% or more treatment retention at 1 year
- Treats craving
- Blocks illicit opioid use
- Over 40 years of research and treatment experience demonstrating effectiveness
- Significantly reduces risk for addiction related death and health problems
- Medication cost is minimal
Limitations of Methadone

- Full agonist with abuse potential
- Potential for dangerous interactions with other drugs when misused
- Highly regulated resulting in limited access to care
- Strong physical dependence results in difficult withdrawal
- Significant stigma in the community
- Heavy burden on patients for compliance
Review of 24 randomized clinical trials with 4,497 patients

Conclusion buprenorphine is superior to placebo and to moderate dose methadone:
- Retaining patients in treatment
- Reducing illicit opioid use
Advantages of Buprenorphine

- Less severe dependency allows for easier transitions between recovery with and without medication
- Partial agonist is safer with less overdose potential
- Lower abuse potential
- People live a normal life free from craving and withdrawal
- SAVES LIVES
Limitations of Buprenorphine

- Not a full agonist and does not retain people in treatment as well as full agonist
- Has diversion potential and may be misused
- Medication is expensive and access is limited
- Stigma in the recovery community
Advantages of Naltrexone

- Safe to use, no abuse potential
- Blocks the effects of opioids
- Reduces danger of accidental overdose
- No physical dependence
- Little or no stigma in the recovery community
Limitations of Naltrexone

- No reinforcing effects to support retention in treatment
- No withdrawal symptoms to prevent treatment drop-out
- May not control cravings
- Must be opioid free for induction, indication is for relapse prevention
# Therapy and Medication

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<thead>
<tr>
<th>Pharmacotherapies</th>
<th>Behavioral therapies</th>
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<tr>
<td>Detoxification</td>
<td>• Set motivation to stop use</td>
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<tr>
<td>Maintenance and stabilization</td>
<td>• Develop alternatives to drug use</td>
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<td>Reduce reinforcement</td>
<td>• Teach coping skills</td>
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<td>Reduce craving/prevent relapse</td>
<td>• Improve interpersonal functioning</td>
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<td>Treat coexisting disorders</td>
<td>• Enhance affect management</td>
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<td>• Enhance compliance with medication</td>
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Limitations of single approaches

Variable efficacy
- Some not helped
- Partial effects

Side effects may limit compliance

Effects fall off with treatment cessation

Treatment efficacy limited to single drug class

Multidimensionality of addicts’ problems

High attrition

No clear superiority of a single approach

Don’t address physiologic aspects of addiction

Variable fidelity
What do we know so far?

- Prescription opioid users tend to have better outcomes than heroin users.
- Most dropout occurs early (first month).
- Early opioid/cocaine positive urines are strong negative predictors of retention/success.
- Dropout usually associated with very poor outcomes.
  - Hence, reasonable to focus on retention as an indicator of better outcomes, but not the whole story.
Neurocognition in Behavioral Addictions

Executive function deficits are greater in those with behavioral addictions than in control subjects, including:

- Planning
- Cognitive flexibility
- Inhibition
QUESTIONS?

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