The Opioid Epidemic: What do we need to know?

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“Synergy: Connect, Communicate, Collaborate”  
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Atlanta, Georgia

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Objectives

1. Learn the history of the opioid epidemic
2. Understand how Opioid Use Disorder is classified in the DSM 5
3. Learn about current treatment for opioid related conditions

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HBO DOCUMENTARY
OVERVIEW OF OPIOID EPIDEMIC

HISTORY OF OPIOIDS

• Opium, the sap of the seed pod of Papaver somniferum, referred to as early as 3000 B.C. and found in Spanish burial sites dated 4200 B.C.
• Greeks and Romans used opium to produce constipation, sleep, and ultimately as a panacea: Hippocrates, Pliny, and Galen
• May be the gall of Scripture (Matt. 27:34)
MORE HISTORY

- Opium use spread from its origins in Turkey with the expansion of Islam.
- Arab traders took it to India and China.
- In Persia, Avicenna (ibn-Sina, 980-1037) recommended opium for eye disease and diarrhea.
- In 1644, the Chinese emperor banned tobacco smoking; Chinese switched to smoking opium.

AND MORE HISTORY

- Arabs trading with Vienna brought opium back to Europe.
- Paracelsus (1493-1541) and Thomas Sydenham, (1624-1689), father of clinical medicine.
- "Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium."

POLITICS AND OPIUM

- British control of opium production in India.
- Usage in Britain climbed during the 1800s.
- Peaked at >10 pounds per 1000 people, 1870.
- Laudanum.
- The Opium Wars (1841, 1856-58, 1860).
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LEGAL CONTROLS OF OPIUM

- The Chinese effort: Opium dens
- Britain’s Pharmacy Act, 1868
- The disease model and the British system
- The American experience: 13 pounds per 1000 people: patent medicines, soldiers’ disease (or army disease) in Civil War
- Laudanum and paregoric
- Harrison Narcotics Act, 1914
- Heroin banned in 1924

OVERVIEW OF OPIOID EPIDEMIC

- Drug overdose deaths and opioid-involved deaths continue to increase in the United States
- More than six out of ten overdoses in the U.S. involve an opioid
- Since 1999, the number of overdose deaths involving opioids quadrupled
- From 2000 to 2015 more than half a million people died from drug overdoses

OVERVIEW OF OPIOID EPIDEMIC

- 115 Americans die every day from an opioid overdose. (CDC 2016)
- The amount of prescription opioids sold to pharmacies, hospitals, and doctors’ offices nearly quadrupled from 1999 to 2010
  - There has not been an overall change in the amount of pain that Americans reported
- Deaths from prescription opioids—drugs like oxycodone, hydrocodone, and methadone—have more than quadrupled since 1999.
OVERVIEW OF OPIOID EPIDEMIC

- Providers wrote nearly a quarter of a billion opioid prescriptions in 2013—enough for every American adult to have their own bottle of pills
- Alabama, wrote almost three times as many of these prescriptions per person as those in the lowest prescribing state, Hawaii
- The most common drugs involved in prescription opioid overdose deaths include:
  - Methadone
  - Oxycodone (such as OxyContin®)
  - Hydrocodone (such as Vicodin®)

GEORGIA’S OPIOID EPIDEMIC

- In Georgia from June 2016 to May 2017, the total number of opioid doses prescribed to Georgia patients surpassed 541 million
  - To put that in perspective, that is approximately 54 doses for every man, woman and child in Georgia
  - Georgia is also among the top 11 states with the most opioid overdose deaths
  - 55 out of the 159 Georgia counties have an overdose rate higher than the national average
WHAT ARE OPIOIDS?

- Powerful pain-relieving drugs
- Derived directly from opium plant or synthesized
- Work at special areas of the brain
- Potentially deadly side effect profile
  - Slow down or stop breathing
  - Induce sleepiness, difficult to arouse
  - Suppressed cough reflex
- Dangerous when taken in combination with alcohol or other substances that depress brain function
  - e.g. anti-anxiety pills; muscle relaxants; anti-depressants

WHAT ARE OPIOIDS?

- Strong Opioids
  - Fentanyl; hydromorphone
  - Actiq®, Fentora®, Oncolis®, Duragesic®, Dilaudid®, Palladone®
- Moderate Strength Opioids
  - Hydrocodone, oxycodone, oxymorphone, morphine, codeine, methadone
  - Vicodin®, Lortab®, Lorcet®, OxyContin®, Percocet®, Percodan®, Tylox®, Combunox®, Opana®, Embeda®, Kadian®, Avinza®, MS Contin®, Norco®, Tylenol-3®
- Weak Opioids
  - Tramadol, pentazocine, propoxyphene, buprenorphine, meperidine
  - Ultram®, Utracet®, Talwin®, Darvocet®, Darvon®, Subutex®, Suboxone®, Demerol®

WHAT ARE OPIOIDS?

- Natural opiates
- Semi-synthetic opiates
- Synthetic opiates
- Opiate antagonists
- Endogenous opiates
**NATURAL AND SEMI-SYNTHETIC**
- Morphine (10% of opium) and codeine, 5%
- Isolated by Frederick Sertturner, 1803
- Injected with invention of hypodermic needle, 1853
- Heroin: Morphine with two acetyl groups
- Diacetylmorphine made by Bayer in 1898, sold as non-addictive
- Dreser, inventor of aspirin, used the same trick of adding an acetyl group to get heroin

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**SYNTHETIC**
- Meperidine (Demerol): Shorter-acting
- Methadone (Dolophine): Orally effective
- Pentazocine (Talwin, 1967)
- Propoxyphene (Darvon)
- Buprenorphine (Buprenex): Partial agonist
- Oxycodone (OxyContin®, Percodan®, Percocet®)
- Hydrocodone (Vicodin®, Lorcet®, 200 generics)

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**OPIATE ANTAGONISTS**

Agonist – Activate Receptors
Antagonists – Block receptors, prevent action of agonists

Pure antagonists
- Naloxone and naltrexone
- Endogenous opiates
- Enkephalins and endorphins
WHAT DO OPIATES DO?

HOW DO OPIATES WORK?

- We are all naturally dependent on opiates for our emotional health and wellbeing.
- Our brains produce natural opiates, **Endorphins** and **Enkalphins** (meaning “in the brain” that help us to maintain emotional equilibrium and to handle pain.
- Pain is one of the main stimulants to the production of these chemicals.
- They are also stimulated by exercise, sex, food (especially chocolate), and even by receiving a compliment.
- Both natural and external opiates operate in the “Pleasure Centers” of the brain.
ANALGESIA – Relieve from Pain

- Nociceptors: Activated by physical or chemical injury or threat of injury
- When stimulated, nociceptive neurons ultimately trigger the release of substance P.
- Opioids, both endogenous and as drugs, inhibit the release of substance P: analgesia.
- Pain information is relayed to the RAS, the thalamus, the somatosensory cortex (for early pain), and the anterior cingulate cortex and the limbic system (for late pain).

BRAIN BLOCKING OF PAIN

- Thalamus, brainstem, and limbic system have many opioid receptors
- Descending neurons travel from sites in the brainstem, such as the PAG, in the raphe (which releases 5-HT) and near the locus ceruleus (which releases NE), in turn activating descending neurons.
- Descending neuron activity inhibits the release of glutamate and substance P in the spinal cord.
- Spinal interneurons release endorphins to inhibit spinal projection neurons.
OPIATE ANALGESIA

- In the spinal cord:
  - On spinal interneurons, morphine mimics endorphins
  - On descending neurons:
    - Directly inhibiting the spinal projection neuron
    - Directly inhibiting the spinal interneuron
    - Directly exciting the inhibitory opioid interneuron

OPIATE ANALGESIA IN THE BRAIN

- Morphine acts on opioid receptors in PAG and raphe
- Activation inhibits cells in the spinal cord
- Locus ceruleus cells normally excite (with NE) spinal pain transmission
- PAG and opioid action on locus ceruleus hyperpolarize and thus inhibit m-receptors

OPIOID RECEPTORS

- Three genetically-controlled sets of receptors: m (mu), k (kappa), and d (delta)
- Mu receptors are in all pain-control areas of the brain and spinal cord, in the respiratory control centers, and nucleus accumbens. Mu receptors respond to morphine and fentanyl (China White).
RECEPTORS...

- Kappa receptors are in pain areas and nucleus accumbens, but also in deeper layers of cerebral cortex. Kappa receptors respond to mixed agonist-antagonists, like pentazocine (Talwin)
- Delta receptors are found in pain areas, nucleus accumbens, and limbic system. They respond to endogenous opiates.

HERE’S HOW OPIOIDS KILL

- In the brain stem, regions called the medulla and the pons control the depth and rate of breathing.
- Both are loaded with opioid receptors — proteins that sit on the surface of cells and grab onto opioids.
- Upon activating, the receptors change the behavior of cells in ways that can slow or even stop breathing.
Substance-related And Addictive Disorders

- Substance Use Disorder
  - Replaces Substance Abuse and Substance Dependence
  - Polysubstance Dependence eliminated
  - New diagnoses related to caffeine and cannabis
- Addictive Disorders
  - Gambling Disorder
    - Only member of new category of behavioral addictions
  - Internet Gaming Disorder also considered for this chapter
    - Placed into “Conditions for Further Study”

Problems with DSM-IV “Abuse” and “Dependence”

- DSM-IV had 2 concepts around substances:
  - “Dependence Syndrome”
  - Abuse: Social and Interpersonal consequences
- Problems:
  - Nearly 50% of all cases of abuse had only one symptom (therefore not a “syndrome”)
  - Abuse implied milder disease, but still had severe consequences
  - Dependence considered higher in hierarchy
    - i.e. No abuse diagnosis if dependence criteria met
    - But not all cases of dependence meet abuse criteria
      - Better reliability if remove hierarchy
    - Abuse not reliably predict development of dependence
      - Factor analysis of abuse and dependence criteria together found just one factor (or 2 highly correlated factors)

Substance Use Disorder

- A maladaptive pattern of substance use manifested as 2 (or more) of the following 11 criteria, occurring within a 12-month period.
- Criteria 1, 2, 3 are the DSM-IV Abuse criteria, dropping the legal problems item.
  - Problems with law enforcement reduced international application

<table>
<thead>
<tr>
<th>DSM IV Substance Abuse Disorder</th>
<th>DSM 5 Substance Use Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Recurrent use causing failure to fulfill major role obligations</td>
<td>1. Same</td>
</tr>
<tr>
<td>2. Recurrent use in hazardous situations</td>
<td>2. Same</td>
</tr>
<tr>
<td>3. Recurrent legal problems due to use</td>
<td>Dropped</td>
</tr>
<tr>
<td>4. Continued use despite social or interpersonal problems caused or exacerbated by use</td>
<td>3. Same</td>
</tr>
</tbody>
</table>
## Substance Use Disorder, cont.

<table>
<thead>
<tr>
<th>DSM IV Substance Dependence</th>
<th>DSM 5 Substance Use Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tolerance: Need more to achieve same effect</td>
<td>4. Same</td>
</tr>
<tr>
<td>2. Characteristic withdrawal syndrome, or use to avoid it.</td>
<td>5. Same</td>
</tr>
<tr>
<td>3. Use for longer or in larger amounts than intended</td>
<td>6. Same</td>
</tr>
<tr>
<td>4. Persistent desire or unsuccessful efforts to cut down use</td>
<td>7. Same</td>
</tr>
<tr>
<td>5. Giving up important activities to use</td>
<td>8. Same</td>
</tr>
<tr>
<td>6. Spending a great deal of time to obtain, use or recover from use.</td>
<td>9. Same</td>
</tr>
<tr>
<td>7. Continued use despite knowing of physical or psychological problem from using</td>
<td>10. Same</td>
</tr>
<tr>
<td></td>
<td>11. Craving to use.</td>
</tr>
</tbody>
</table>

### DSM IV vs 5 Substance Use Disorders

<table>
<thead>
<tr>
<th>DSM IV Abuse*</th>
<th>DSM IV Dependence*</th>
<th>DSM 5 Substance Use Disorder*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social/personal problems related to use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sense of loss and lack of control over use</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Legal problems</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Tolerance</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Used larger amounts/larger</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Impaired control over use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Much time spent using</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Physical/psychological problems related to use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Activities given up to use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Craving</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Withdrawal not included for cannabis, inhalant, and hallucinogen disorders in DSM-IV. Cannabis withdrawal added in DSM-5.

### Changes in DSM 5

- Abuse/Dependence gone
- Replaced by:
  - Alcohol Use Disorders
  - Cocaine Use Disorders
  - Opioid Use Disorders
- Criteria set are similar but expanded to 11.
- Must have 2 in 12 month period
### Substance Use vs Substance Induce

**Substance Induce Disorder:**
- Intoxication
- Withdrawal
- Other substance/med. induced mental disorders

### Substance Use Disorder

- Craving
  - Did not meaningfully impact diagnostic criteria
  - Included because it may become focus of future treatment
- Threshold of 2 criteria
  - Maximized agreement with combined DSM-IV substance abuse + dependence prevalence
  - If on prescribed psychoactive medication, tolerance and withdrawal do not count toward the criteria


### Substance Use Disorder - Specifiers

- **Eliminated “Partial/Full remission”**
  1. “Remission” = Not meeting S.U.D. criteria except craving
     - “Early”: ≥3 and <12 months
     - “Sustained”: ≥12 months
  2. “On Maintenance Therapy”
     - Replaces “On agonist therapy”
     - E.g. Methadone; Buprenorphine; Natrexone; Varenicline; Bupropion
  3. “In a Controlled Environment”
     - Same as DSM-IV
Severity Levels for Substance Use Disorder

• 2-3 criteria: Mild
• 4-5 criteria: Moderate
• 6+ criteria: Severe

DSM 5: Opioid Related Disorders

• Opioid use dis.
• Opioid intoxication
• Opioid withdrawal
• Other opioid-induced dis.
• Unspecified opioid-related dis.

Opioid Use Disorder

Diagnostic Criteria:
1. Opioids taken in larger amounts than intended
2. Unsuccessful efforts to control use
3. Time spent acquiring/recovering from opioids
4. Craving to use
5. Recurrent use despite adverse effect on work/home
6. Use despite recurrent interpersonal problems
7. Important social/occupational/recreational activities given up
8. Use where physically hazardous
Opioid Use Disorder (cont..)

9. Using despite awareness of its adverse physical/psychological consequences

10. Tolerance (either):
   a. Need higher dose overtime
   b. Markedly diminished effect by same dose
(Tolerance is not met if taking meds under medical supervision.)

11. Withdrawal manifested by (either):
   a. Classic opioid withdrawal symptoms
   b. Opioids (or similar) used to avoid withdrawal
(Withdrawal is not met if taking meds under medical supervision.)

Opioid Related Disorder

Level of severity:

<table>
<thead>
<tr>
<th>DSM 5</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (2-3)</td>
<td>305.50</td>
</tr>
<tr>
<td>Moderate (4-5)</td>
<td>304.00</td>
</tr>
<tr>
<td>Severe (6+)</td>
<td>304.00</td>
</tr>
</tbody>
</table>

Opioid Related Disorders

Specifiers:
In early remission
– No criteria met for 3 months but less than 12
In sustained remission
– No criteria met for 12 months except “craving”
On maintenance therapy
– Suboxone, methadone
In controlled environment
TREATMENT FOR OPIOID USE DISORDERS

Substance-related and Addictive Disorders Personnel

- Licensed/Certified Addiction Counselors
- Person Centered Case Managers
- Recovery Coaches
- Peer Mentors
- Certified Peer and Recovery Support Specialists

Substance-related and Addictive Disorders Services

- Universal Screening
- SBIRT
- Inpatient, Outpatient
- Individual, group, family therapy
- Recovery Coaching
- Warm Lines
- Full Bio-psycho-social assessment
TYPICAL PRESENTATION AND COURSE

- Present in acute intoxication, acute/chronic withdrawal or substance induced mood, cognitive disorder or medical complications
- Abstinence depends on several factors: social, environmental, internal factors (presence of other comorbid psychiatric illnesses)
- Remission and relapses are the rule (just like any other chronic medical illness)
- Frequency, intensity and duration of treatment predicts outcome
- 70% eventually able to abstain or decrease use to not meet criteria

TREATMENT

- Manage Intoxication & Withdrawal
  - Intoxication
    - Ranges: euphoria to life-threatening emergency
  - Detoxification
    - outpatient: "social detox" program
    - inpatient: close medical care
    - preparation for ongoing treatment

ACUTE INTERVENTION

- Overdose
  - Emergency
  - Support vital signs
  - Naloxone: 0.4 mg q 2-3 min. SC/IV
- Withdrawal
  - Rating scales: CINA, COWS
  - Opioid substitution with gradual decrease
  - Symptomatic treatment
OPTIONS FOR WHERE TO TREAT

- Hospitalization:
  - Due to drug OD, risk of severe withdrawal, medical comorbidities, requires restricted access to drugs, psychiatric illness with suicidal ideation
- Residential treatment unit:
  - No intensive medical/psychiatric monitoring needs
  - Require a restricted environment
  - Partial hospitalization
- Outpatient Program:
  - No risk of med/psych morbidity and highly motivated patient

PHARMACOLOGICAL TREATMENT

1. Methadone
   - Full µ agonists
   - Once/day dosed
   - 40-60 mg/d: sufficient to block withdrawal sx.
2. Buprenorphine/Naloxone
   - µ Receptor partial agonist
   - Kappa receptor partial antagonist
   - 12-16 mg/d
   - Combination ↓ risk of diversion

<table>
<thead>
<tr>
<th>Medicine</th>
<th>µ agonist</th>
<th>Partial agonist</th>
<th>Antagonist</th>
<th>MPR</th>
<th>µ antagonist</th>
<th>Kappa antagonist</th>
<th>Clinical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Full</td>
<td>Partial</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Full µ agonist, high efficacy, High safety, High demand, High potential for abuse, High addiction risk, High treatment risk, High cost, High risk of diversion</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Partial</td>
<td>Partial</td>
<td>Partial</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>µ Receptor partial agonist, Kappa receptor partial antagonist, Partial µ agonist, Partial Kappa antagonist, Partial µ antagonist, Partial Kappa antagonist, Partial clinical use</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>µ Antagonist, Kappa Antagonist, Partial µ antagonist, Partial Kappa antagonist, Partial clinical use</td>
</tr>
</tbody>
</table>

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PSYCHOSOCIAL TREATMENT

- Specialized programs
- Cognitive behavioral therapy
- Behavioral therapy
- Psychodynamic/interpersonal
- Recovery-oriented therapies
- Group and Family therapy
- Self-help groups: NA, Al-Anon

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Thank You

Mahalo

Kiitos

Obrigado

Gracias

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