Treatment of Opioid Use Disorder

Casia Horseman, MD
Assistant Professor
Department of Psychiatry and Behavioral Health
The Ohio State University Wexner Medical Center

Objectives

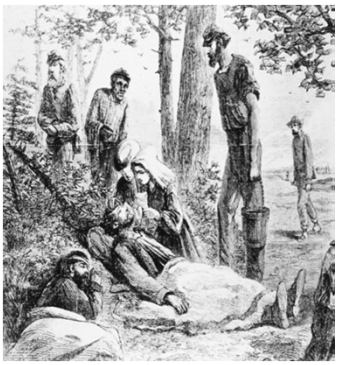
- **Discuss the historical context of opioid use and current medical view of addiction**
- **Review the epidemiology of the opioid epidemic**
- **Describe the DSM-5 criteria for Opioid Use Disorder, Opioid Intoxication, and Opioid Withdrawal**
- **Review the assessment of Opioid Use Disorder**
- **Describe the treatment settings for Opioid Use Disorder**
- **Describe pharmacological and psychosocial treatments for Opioid Use Disorder**

Opioids

- **Opium-derived or synthetic compounds used medically for the relief of pain.**
- **Many opioids have the potential for misuse.**
- **Opioids have been used and misused for thousands of years world wide.**

Historical Context of Opioid Use

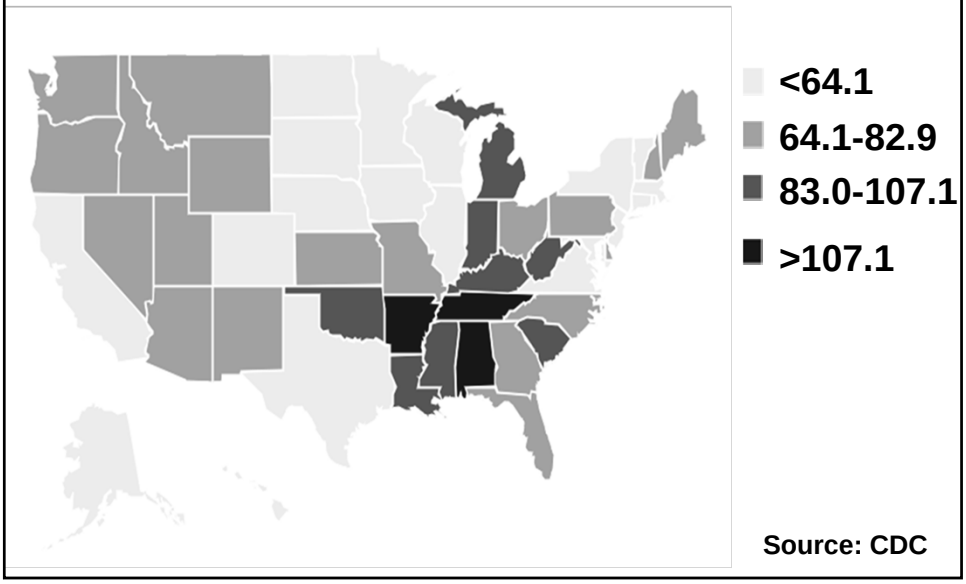
- **Morphine entered into widespread use during the US Civil War.**
- **Increased morphine use lead to addiction among the upper social class**
- **Increasing rates of addiction led to restrictive laws and policies which effectively criminalized addiction.**
- **Harrison Narcotics Act (1914) prohibited prescribing of narcotics (opioids) to addicts. Physicians decreased prescribing for fear of prosecution.**



Culture Change 1990s-2000s

- Strong emphasis on treatment of pain
- Widespread belief that those with pain were less likely to abuse opioids
- New potent opioids developed and aggressively marketed
- Supply of opioids increased markedly
- Pain Management Standards became effective Jan. 1, 2001, via the Joint Commission
- Simultaneously, the rates of addiction to opioids and death rates due to overdose also increased

Opioid prescriptions per 100 people by state 2016



Source: CDC

Addiction

- **Non-specific term frequently used to refer to a variety of substance-related disorders & compulsive behaviors**
- **Not just physiological dependence**
- **Present when there is a pattern of pathologic use**
- **A pattern of behavior with social, occupational, and interpersonal consequences**

Definition of Addiction

"Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. It is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death."

American Society of Addiction Medicine, 2011

DSM-5 Opioid Use Disorder Criteria

A. A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring 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 the opioid, use the opioid, or recover from its effects.**
4. **Craving, or a strong desire or urge to use opioids.**

DSM-5 Opioid Use Disorder Criteria

5. **Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.**
6. **Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.**
7. **Important social, occupational, or recreational activities are given up or reduced because of opioid use.**
8. **Recurrent opioid use in situations in which it is physically hazardous.**
9. **Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.**

DSM-5 Opioid Use Disorder Criteria

10. Tolerance, as defined by either of the following:

a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.

b. A markedly diminished effect with continued use of the same amount of an opioid.

11. Withdrawal, as manifested by either of the following:

a. The characteristic opioid withdrawal syndrome.

b. Opioids (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

Notes Regarding the Criteria

- **Criteria are grouped according to similar symptoms:**
  - **Criteria 1-4: Impaired control**
  - **Criteria 5-7: Social impairment**
  - **Criteria 8-9: Risky use**
  - **Criteria 10-11: Pharmacological criteria**
- **Symptoms of tolerance and withdrawal occurring during appropriate medical treatment with prescribed medications are specifically *not* counted when diagnosing a substance use disorder.**
- **A substance use disorder can be correctly diagnosed for prescribed medication when there are other symptoms of compulsive, drug-seeking behavior**

DSM-5 OUD Specifiers

- In early remission
  - 3-12 months without symptoms (except craving)
- In sustained remission
  - More than 12 months without symptoms (except craving)
- On maintenance therapy (includes agonists and antagonists)
- In a controlled environment

DSM-5 Opioid Intoxication Criteria

A. Recent use of an opioid.

B. Clinically significant problematic behavioral or psychological changes that developed during, or shortly after, opioid use.

C. Pupillary constriction (or pupillary dilation due to anoxia from severe overdose) and one (or more) of the following signs or symptoms developing during, or shortly after, opioid use:

1. Drowsiness or coma.
2. Slurred speech.
3. Impairment in attention or memory.

DSM-5 Opioid Intoxication Criteria

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

***Specify* if: With perceptual disturbances: This specifier may be noted in the rare instance in which hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium.**

DSM-5 Opioid Withdrawal Criteria

A. Presence of either of the following:

A. Cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e., several weeks or longer).

B. Administration of an opioid antagonist after a period of opioid use.

DSM-5 Opioid Withdrawal Criteria

B. Three (or more) of the following developing within minutes to several days after Criterion A:

1. **Dysphoric mood.**
2. **Nausea or vomiting.**
3. **Muscle aches.**
4. **Lacrimation or rhinorrhea.**
5. **Pupillary dilation, piloerection, or sweating.**
6. **Diarrhea.**
7. **Yawning.**
8. **Fever.**
9. **Insomnia.**

DSM-5 Opioid Withdrawal Criteria

C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Opioid Withdrawal

- **Short-acting opioids (e.g., heroin, hydrocodone, oxycodone)**
  - **Usually begins 6-12 hours after last dose**
  - **Peaks at 36-72 hours**
  - **Lasts about 5 days**
  - **Possible protracted withdrawal (PAWS)**
- **Opioids with longer half-lives (e.g., methadone)**
  - **longer period before withdrawal onset**
    - **methadone: 24-48 hours**
  - **longer period before peak withdrawal symptoms occur**

Opioid Withdrawal

- **Opioid intoxication IS life-threatening**
- **Opioid withdrawal IS NOT life threatening, but is exceedingly uncomfortable**
- **If respiratory compromise or seizures**
  - **Always consider use of other drugs and treat if needed**
    - **Sedative hypnotic withdrawal can be life-threatening**

Treatment Objectives

- **Establish & maintain therapeutic alliance**
- **Assess safety & clinical status**
- **Manage intoxication & withdrawal**
- **Develop treatment plan**
- **Educate patient re: substance use disorders**
- **Motivate the patient to change**
- **Prevent relapse**
- **Reduce morbidity & sequelae**

SBIRT

- **Evidence-based practice to identify, reduce, and prevent problematic use, abuse, and dependence on substances which can occur in any healthcare setting.**
  - **Screening**
    - **Assess for risky substance use behavior with standardized screening tools.**
  - **Brief Intervention**
    - **Engage patient showing risky substance use behaviors in a short conversation, providing feedback and advice.**
    - **Goal to increase insight and awareness of the risks as well as motivation toward behavioral change**
  - **Referral to Treatment**
    - **Provide a referral to brief therapy or additional treatment.**

Screening

- Ask about substance use using open ended questions
- Follow up on any positive responses with formal tool or more intensive interview
  - Alcohol, Smoking, and Substance Involved Screening Test (ASSIST) or NIDA-Modified ASSIST
  - Drug Abuse Screening Test (DAST)
- Consider point of care testing

Brief Intervention

- Goal can range from increasing awareness of risk to reducing or eliminating use
- Understanding Stages of Change
  - Precontemplation, contemplation, determination, action, maintenance
  - Patients are in different stages based on readiness or motivation to change
    - Interventions should be tailored accordingly
  - Not a linear process
    - Patients cycle through stages before mastering behaviors they want to change
- Motivational Interviewing

Brief Intervention

- **FRAMES Method**
  - **offer Feedback**
  - **emphasize personal Responsibility**
  - **give Advice**
  - **provide a Menu of options**
  - **use Empathy**
  - **support Self-efficacy**

Assessment of Opioid Use Disorder

- **Should be completed by a trained, licensed/certified professional**
- **Should display positive, non-confrontational interaction**
- **Longitudinal assessment, collateral information**
- **Always inquire about use of other drugs**
  - **Frequency, duration of use, withdrawal**
- **Past treatment history (what helped, what didn't)**
- **Level of insight and motivation (Stages of change)**

Medical Interview

- Chief complaint
- Present illness
  - Substances used, frequency, route, problems caused by use
- Medical history
  - Conditions needing opioids—dental, back pain, post-surgical
- Psychiatric history
  - History of overdose, suicide attempts

Medical Interview

- Medications (controlled drugs)
- Allergies
  - Consider multiple allergies to non-narcotic or controlled medications
- Family history
  - Addiction, suicide, medical complications (cirrhosis, hepatitis, etc.)
- Social history
  - Legal issues, child protective services, other users of substances
- Review of systems
- Prescription Monitoring Program

Physical Findings

- **Unexplained bruises and abrasions**
- **Frequent trauma**
- **Slurred speech**
- **Constricted pupils**
- **Memory deficits**
- **Track marks**
- **Jaundice**
- **Murmurs**

Lab Analysis

- **Opioids detected in blood, urine, saliva, and hair**
- **Increased mean corpuscular volume (MCV)**
- **Increased liver enzymes (GTT, SGOT, SGPT)**
- **Elevated triglycerides, HDL**
- **Elevated uric acid**
- **Drug screen/ blood alcohol concentration**
- **Hepatitis serology, HIV testing, etc.**

Urine Toxicology Screen

- **Random Urine Toxicology Screening: Gold standard**
  - **Heroin is excreted in urine as morphine**
  - **6-monoacetyl morphine (6-MAM) detected for 12 hours – evidence of recent heroin use**
- **Person receiving results should understand limitations of testing**
  - **Routine opiate screens may not detect meperidine, oxycodone, fentanyl, tramadol, buprenorphine, methadone**
  - **Poppy seeds contain trace amounts of codeine and morphine and can give positive result.**

Treatment Settings

- **Inpatient Hospitalization**
- **Residential Treatment Programs**
- **Partial Hospitalization**
- **Outpatient Treatment**
  - **Intensive Outpatient Programs**
  - **Outpatient counseling**
- **Medication Assisted Treatment (MAT)**

Opioid Use Disorder Treatment Overview

- Acute and maintenance phases of treatment
  - Medical detoxification (acute)
    - Tapering the substance itself or by substituting then tapering a closely related substance
    - Standardized scales to monitor withdrawal (COWS, OOWS)
    - Risk of overdose with decrease in tolerance following treatment
  - Minimize relapse risks (maintenance)
    - Relapse rates high (90%) following detoxification with no medication treatment
    - Pharmacologic interventions - agonist or antagonist treatment
  - Psychosocial interventions (acute and maintenance)

Inpatient treatment

- Goal is to stabilize acute medical and psychiatric crises
- Hospitalization with around the clock medical management
- Most intensive level of care and usually short duration
- Management of detoxification or other medical or psychiatric crises

Candidates for Inpatient Treatment

- **Patients with**
  - **Severe overdoses, severe respiratory depression or coma**
  - **Severe withdrawal syndromes complicated by multiple drugs**
  - **Withdrawal complicated by acute or chronic general medical conditions**
  - **Severe psychiatric comorbidity making them a danger to self or others**
  - **History of nonresponse to less intensive form of treatment**

Detoxification Treatment Goals

- **Resolve medical and psychiatric problems associated with withdrawal**
- **Prevent the development of complications of withdrawal**
- **Stop the patient's pattern of abusive substance use during and following detox**
- **Enhance factors which promote sobriety**
- **Minimize factors which detract from sobriety**
- **Engage the patient in formal rehabilitation**
- **Prevent the need for repeated detoxification**

Medical Detoxification

- Opioid detoxification
  - Stabilize on methadone and taper
    - Must be done at narcotic treatment programs
    - Could be done in emergency situation when patient is hospitalized for other urgent medical problem
  - Stabilize on buprenorphine and taper
    - Can be done inpatient or outpatient by a waivered physician

Medical Detoxification

- Non-opioid detoxification
  - Clonidine
    - Alpha-2 adrenergic agonists suppress autonomic symptoms caused by opioid withdrawal
    - Limiting side effect is hypotension
- Ultra-rapid opioid withdrawal
  - Deep sedation and administer opioid antagonist to provoke withdrawal
  - Withdrawal reportedly resolves in 2-3 days with patient on full dose of antagonist (naltrexone) if patient completes treatment; high drop-out rate
  - Risk of serious adverse events: aspiration pneumonia, renal failure, death

Residential Treatment

- Live-in facility with 24 hour supervision
- Goal is to offer stable, structured, therapeutic environment
- May offer medical monitoring for detoxification
- Can vary in whether they provide medication assisted treatment
- Can range in duration from 28 days to months or years
- Can range in intensity from self-contained therapeutic communities to halfway houses

Candidates for Residential Treatment

- Patients who
  - Do not meet criteria for hospitalization
  - Lack social supports or motivation to maintain sobriety as an outpatient
  - Have lack of transportation as a barrier to attending outpatient levels of care
  - Have unstable housing or a living situation that hinders the ability to maintain sobriety

Intensive Outpatient Treatment/Partial Hospitalization

- 9-30 hours per week
- Ranges from 3 to 7 sessions per week (3-8 hours per session)
  - Frequency and duration generally tapered as patients display increasing stability
- Goal is to provide more structure and support than traditional outpatient care
- Generally is group treatment

Candidates for PHP/IOP

- Patients who
  - Can maintain sobriety without full time supervision
  - Have some social support but require additional structure
  - Are early in treatment and could benefit from intensive education
  - Are transitioning from hospital or residential settings

Outpatient Treatment

- Least intensive level of care
- Less than 9 hours of scheduled attendance per week
- Can include individual counseling, group counseling, family counseling, medication management visits
- Can be used for primary intervention or extended aftercare

Candidates for Outpatient Treatment

- Patients who
  - Have appropriate support systems
  - Have adequate living arrangements
  - Have transportation to services
  - Have motivation to regularly attend treatment

Medication Assisted Treatment Options

- Methadone
  - Long acting mu agonist
- Buprenorphine
  - Mu partial agonist/antagonist
  - Kappa antagonist
- Naltrexone
  - Mu antagonist
- Long acting injectable naltrexone (Vivitrol)
  - Used monthly

Agonist Treatment

- Use of a long acting medication in the same class as the abused drug (once daily dosing)
  - Prevention of Withdrawal Syndrome
  - Lifestyle stabilization
    - Improved health and nutritional status
    - Decrease in criminal behavior
    - Employment
    - Decrease in injection drug use/shared needles

Methadone

- Full opioid agonist.
- Highly regulated schedule II drug
  - Only available through federally approved facilities.
- Daily doses initially.
- Slow titration to therapeutic dose.
- Can cause respiratory depression and death if increased too quickly or taken in overdose.
- Cardiac risk : QT prolongation
  - Check ECG before initiating and after 30 days
- Approved for use in pregnancy

Buprenorphine

- Available by prescription.
  - Only agonist medication approved for treatment of OUD in office based setting
  - Prescribers are required to have additional training and special waiver
- Mixed opioid agonist-antagonist.
  - Can precipitate withdrawal unless patients is already in moderate withdrawal.
  - Effectiveness may be limited in very heavy opioid users
- Therapeutic dose usually reached in 24-48 hours.
- Less risk of respiratory depression and death in overdose.

Buprenorphine Formulations

- Buprenorphine/naloxone
  - Naloxone is a full antagonist (Narcan)- included so patients cannot use IV
  - Most common form is films or tablets for sublingual administration (Suboxone, Zubsolv)
  - Also available in buccal film (Bunavail)
- Buprenorphine
  - Most common form is tablet for sublingual administration (Subutex)
    - Primarily used for pregnant patients
  - Long acting monthly injection (Sublocade)
  - Implant for up to 6 months recently approved (Probuphine)

Antagonist Treatment

- Use of receptor blocker to block agonist effects of a dose of opioid
- Prevent impulsive use of drug
- Consider compliance: works well in motivated patients

Naltrexone

- Opioid receptor blocker
- Available in daily tablet or monthly injection (Vivitrol)
- Side effects: hepatotoxicity
  - Monitor liver function tests every 3 months
- Risk of overdose if 'overcome' naltrexone

Psychosocial Interventions

- Presented in individual or group settings in all levels of care
- Evidence based interventions:
  - Cognitive behavioral therapy and other behavioral therapies
  - Motivational enhancement therapy
  - 12-Step facilitation
  - Psychodynamic therapy
  - Interpersonal therapy
  - Self help manuals
  - Case management
  - Marital and family therapy

Additional Considerations Regarding Treatment

- Like other chronic medical illnesses, there is no “one size fits all” treatment.
- Mutual aid groups (AA/NA) alone is not considered treatment
  - Can be an important adjunct to treatment
- It is important to include patients’ family/significant other if possible
- There is a significant treatment gap
  - Only about 10% of people in need of treatment receive it

References

1. American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.
2. Center for Substance Abuse Treatment. *Clinical Guidelines for the use of Buprenorphine in the Treatment of Opioid Addiction*. Treatment Improvement Protocol (TIP) Series 40. DHHS Publication No. (SMA) 04-3939. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2004.
3. Center for Substance Abuse Treatment. *A Guide to Substance Abuse Services for Primary Care Physicians*. Treatment Improvement Protocol (TIP) Series 24. DHHS Publication No. (SMA) 08-4075. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2008.
4. Centers for Disease Control and Prevention. U.S. State Prescribing Rates, 2016 [Map]. Retrieved April 20, 2018 from https://www.cdc.gov/drugoverdose/maps/rxstate2016.html.
5. Courtwright, David T. *Dark Paradise: A History of Opiate Addiction in America*. Cambridge, Mass: Harvard University Press, 2009.
6. Lipari, R. N., Park-Lee, E., and Van Horn, S. *America’s need for and receipt of substance use treatment in 2015*. The CBHSQ Report: September 29, 2016. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Rockville, MD.
7. Ries, R. K., Fiellin, D. A., Miller, S. C., & Saitz, R. (2014). *The ASAM principles of addiction medicine: Fifth edition*. Wolters Kluwer Health Adis (ESP).