

AN EXPLORATION OF WITHDRAWAL

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Objectives

1. Identify drug classes, medications, and substances that are commonly associated with withdrawal.
2. Describe common symptoms associated with withdrawal syndromes.
3. Identify psychosocial, behavioral, and medical issues related to withdrawal.

What is withdrawal?

- A set of symptoms that occur when consistent use of a substance is suddenly stopped.
- Withdrawal symptoms are typically the opposite of effects seen when substance is used

What is withdrawal?

- Ongoing or long-term substance use causes the body to adapt.
- Then, ongoing use of the substance is required in order to maintain ordinary functions in the body.
- When the substance is suddenly stopped, the “new normal” balance is disrupted.
- The body’s adaptations remain and continue unchecked, causing withdrawal symptoms

Substance “abuse”

- **Substance abuse** – *“A maladaptive pattern of substance use leading to clinically significant impairment or distress” – DSM-IV*
 - Widely used term
 - Complex connotations and stigma
 - No longer in Diagnostic and Statistical Manual of Mental Disorders
- General shift toward **“substance use disorder”**

CATEGORIES OF SUD SYMPTOMS

Symptoms of substance use disorders in the DSM 5 fall into four categories: 1) impaired control; 2) social problems; 3) risky use, and 4) physical dependence.

Impaired Control	Social Problems	Risky Use	Physical Dependence
Using more of a substance or more often than intended Wanting to cut down or stop using but not being able to	Neglecting responsibilities and relationships Giving up activities they used to care about because of their substance use Inability to complete tasks at home, school or work	Using in risky settings Continued use despite known problems	Needing more of the substance to get the same effect (tolerance) Having withdrawal symptoms when a substance isn't used

Factors & Circumstances

- Ran out of Rx medication
- New job/new health insurance
- Lost job/lost health insurance
- Transportation issues to pick up Rx
- Moved
- Medications/drugs lost or stolen
- Medications/drugs removed from the home
- Hospitalization
- Street drugs not what you thought
- New dealer/supplier
- Medications/drugs discontinued by provider
- Seeing a new doctor or care team
- Jail/prison
- Voluntary cessation, trying to quit
- Antidote/reversal agents

Withdrawal, Dependence, and Addiction: A Complex Relationship

- Many patients will require:
 - Medical care for symptoms of withdrawal (emergency, hospitalization, or outpatient)
 - Addiction & recovery treatment (inpatient or outpatient)
 - Ongoing recovery support
 - +/- medical care for their other disease states that precipitated, or were brought on by, their substance use
 - Chronic pain
 - Psychiatric disorders such as depression, bipolar, anxiety, PTSD, etc
 - Infection (HIV, Hep C, others)

Dependence & addiction

- **(Physical) dependence** occurs when the body/brain begins to rely on an external substance to maintain normal function
 - **Tolerance:** needing ever-increasing doses to maintain normal function
 - With dependence, reducing/quitting the substance leads to **withdrawal** (range of symptoms)
- **Addiction:** when dependence becomes disruptive to other aspects of life (dependence is a symptom of addiction)

The background features a repeating pattern of small, light blue triangles. Overlaid on this are four stylized white pills and capsules. Two are capsules with a vertical score line, one is positioned above and one below the text. Two are round tablets with a horizontal score line, one is positioned above and one below the text.

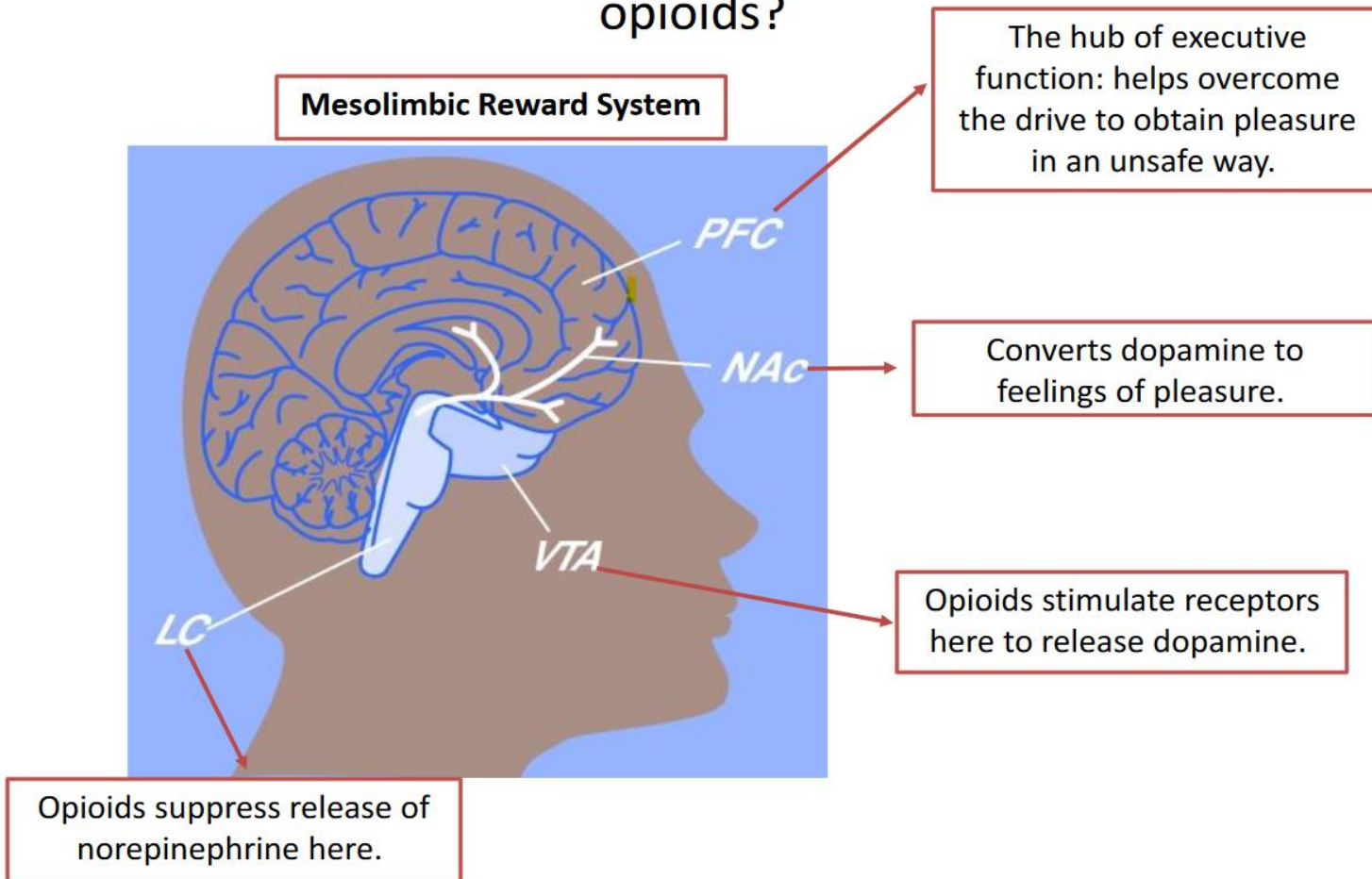
Opioids & Opiates

Opioid (physical) dependence



Opioid (physical) dependence

Structural changes: How do people become addicted to opioids?



- Produces feelings of pleasure and euphoria → reinforces behavior → dependence
- With enough opioid use, the most primal part of the brain can see opioids as necessary for survival

Opiates & Opioids Withdrawal

- Includes:
 - Oxycodone
 - Hydrocodone
 - Heroin
 - Morphine
 - Fentanyl
 - Others
- **Mechanism:** Opioid receptors in central nervous system

Withdrawal Symptoms

- Anxiety
- Restlessness/agitation
- Nausea, vomiting, diarrhea
- Diaphoresis (sweating)
- Tachycardia (rapid heart rate)
- Tremors (shaking)
- Flu-like symptoms: runny nose/eyes

Opiates & Opioids Withdrawal

- Onset: 6-12 hours after last use
- Duration: 5-10 days
- Withdrawal Treatments
 - Medications
 - Alpha-blocker (Lucemyra)
 - Symptomatic treatments
 - Tapers

Taper: Slowly decreasing or increasing a dosage over a period of time until the desired dosage is reached



Opiates & Opioids Withdrawal

Agonist: Attaches to a receptor and activate(stimulates) a receptor

Antagonist: Attaches and blocks interaction to a receptor

Agonist examples:

- Oxycontin, Heroin, and Fentanyl

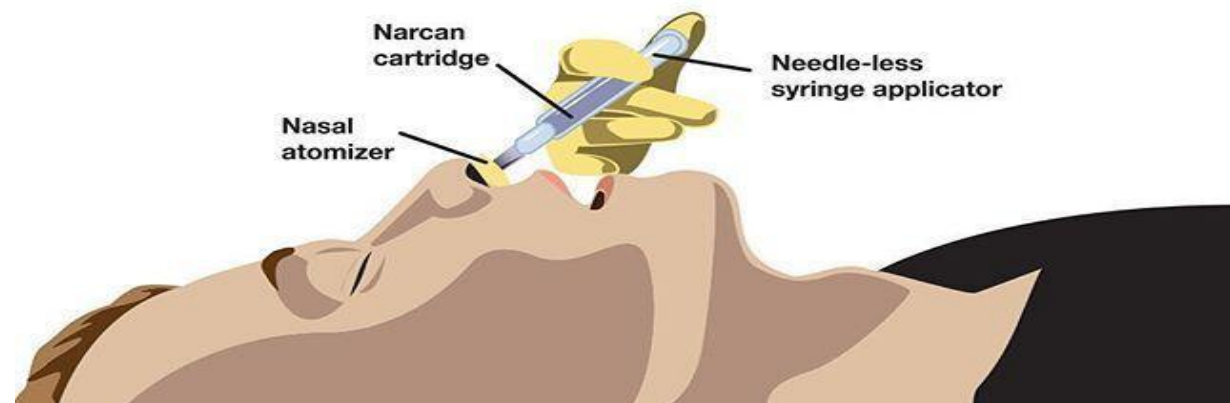
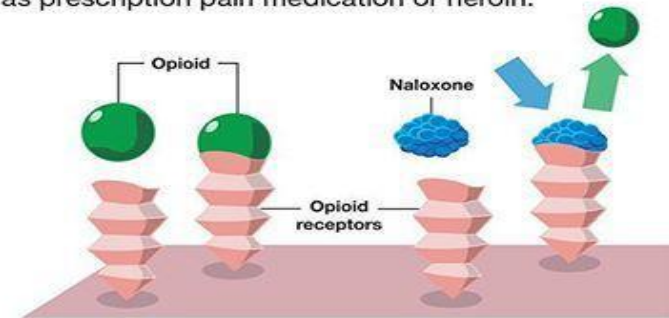
Antagonist example

- Naloxone (Narcan)

Naloxone (Narcan)

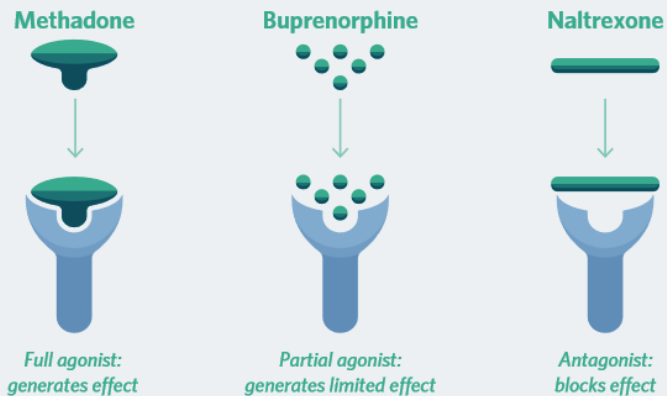
What Is It? Naloxone is a medication that can reverse an overdose that is caused by an opioid drug such as prescription pain medication or heroin.

How Does It Work?
When administered during an overdose, naloxone blocks the effects of opioids on the brain and restores breathing within two to eight minutes to prevent death.



Opiates & Opioids – MOUD/MAT

Figure 1
How OUD Medications Work in the Brain



- Medication for Opioid Use Disorder (MOUD)
 - Methadone (Full Agonist)
 - Buprenorphine (Partial Agonist)
 - Buprenorphine/Naltrexone “Suboxone” (Agonist/Antagonist)
 - Naltrexone (Antagonist)
- Goal is to stabilize and sustain patient on new drug and then taper off
- Medical Assisted Treatment (MAT) is when medication is combined with behavioral treatment

Opiates & Opioids – Kratom

- **Kratom**

- Plant from Southeast Asia
- Contains compounds that are opioids
- Legal and readily available in most of the US; little regulation
- Used and misused for effects similar to opioids



Opiates & Opioids – Kratom



- **Kratom**

- Withdrawal is similar to other opioids
- Sometimes used by those struggling with substance use disorder as a substitute or to avoid withdrawals

Opiates & Opioids – Loperamide



- **Loperamide (Imodium)**
 - Anti-diarrhea medication available OTC
 - **Mechanism:** Targets some opioid receptors, mainly gastrointestinal
 - Used in large quantities to prevent/mitigate opioid withdrawal symptoms
 - Severe cardiac effects may occur when consuming large quantities

Naloxone

- Used to reverse opioid overdose/toxicity; life saving
- Available in WA via the Statewide Standing Order to Dispense Naloxone



STANDING ORDER TO DISPENSE NALOXONE

Authority: This standing order is issued in accordance with RCW 69.41.095(5), which allows for "[t]he secretary or the secretary's designee [to] issue a standing order prescribing opioid overdose reversal medications to any person at risk of experiencing an opioid-related overdose or any person or entity in a position to assist a person at risk of experiencing an opioid-related overdose."
The physician issuing this standing order has been designated to do so by the Secretary of Health.

Purpose: The purpose of this standing order is to aid persons experiencing an opioid related overdose by facilitating distribution of the opioid antagonist naloxone to people in Washington

Naloxone

- After receiving naloxone, the patient may immediately experience withdrawal symptoms:
 - nausea/vomiting, chills, muscle aches
- Always call 911 when giving naloxone, even if the patient wakes up & feels ok

Who should carry naloxone?

- People who use drugs
- People who know people who use drugs
- Anyone on opioids (especially those on high doses)
- Anyone using drugs not purchased at a pharmacy or dispensary
- Anyone!

Other Substances

Benzodiazepines (BZD) Withdrawal

- Includes:
 - clonazepam (Klonopin)
 - alprazolam (Xanax)
 - diazepam (Valium)
 - lorazepam (Ativan)
 - chlordiazepoxide (Librium)
 - others
- **Mechanism:** Complex pathways involving the neurotransmitter GABA



Benzodiazepines (BZD) Withdrawal

Withdrawal symptoms

- Anxiety
- Confusion
- Psychosis
- Tremors
- Seizures

Half-life: The time it takes for the amount of a substance in the body to decrease by half

- **Benzodiazepine withdrawal can be life threatening**
- **Onset:** within 1-21 days after last dose depending on half-life
 - Withdrawal from *short-acting* benzodiazepines occurs more quickly
 - Withdrawal from *long-acting* benzodiazepines may be delayed
- **Duration:** weeks to months
- **Withdrawal treatment:**
 - Provider may switch to a long-acting benzodiazepine
 - Discontinue via a very slow taper over months

Benzodiazepines (BZD) Withdrawal

- Withdrawal treatment options
 - Switch to a long-acting benzodiazepine with a long duration of effect
 - Discontinue via a very slow taper over a period of months
 - Seizure prevention
- Note: Flumazenil (Romazicon) for BZD toxicity/overdose is **NOT RECOMMENDED**
 - Reversal agent for benzodiazepine toxicity and overdose
 - May precipitate withdrawal symptoms, including seizures

Gamma-Hydroxybutyrate (GHB) Withdrawal

Withdrawal symptoms

- Agitation
- Tremor
- Tachycardia
- Hypertension
- Insomnia
- Delirium
- Seizures

- *Mechanism:* GABA receptors
- Treatment
 - Benzodiazepines
 - Baclofen
 - Barbiturates
 - Propofol
 - GHB

Alcohol (Ethanol) Withdrawal

- **Mechanism:**
 - Alcohol acts on GABA receptors and inhibits excitatory effects in the brain
 - Chronic use causes brain adaptations in these pathways
 - When alcohol is suddenly stopped, the balance is disrupted and excessive/overactivity of the central nervous system occurs
- **Alcohol withdrawal can be life threatening**



Alcohol (Ethanol) Withdrawal

Withdrawal symptoms:

- Tremors (shaking)
- Anxiety, nervousness, agitation
- GI upset (nausea, retching, vomiting)
- Headache
- Diaphoresis (sweating)
- Confusion
- Hallucinations (seeing/feeling things that aren't there)
- Seizures
- Delirium tremens or "DTs" (hallucinations, disorientation, tachycardia, hypertension, hyperthermia, diaphoresis)
 - May occur 2-4 days after last drink

Alcohol (Ethanol) Withdrawal



- **Onset:** ~6 hours
 - May begin as soon as 2 hours after last drink
 - May occur even before blood alcohol level reaches 0
- **Duration:** as long as 5-7 days
- **Treatment:**
 - Benzodiazepines to alleviate symptoms
 - Correct any metabolic disturbances (acid/base, electrolytes, other)
 - Nutritional support (thiamine, folic acid, multivitamins, aka “*banana bag*”)

Clinical Institute Withdrawal Assessment for Alcohol (CIWA)

Scoring on a scale from 0-7 for each symptom:

1. Agitation (0-7)
2. Anxiety (0-7)
3. Auditory disturbances (0-7)
4. Clouding of sensorium (0-7)
5. Headache (0-7)
6. Nausea/vomiting (0-7)
7. Paroxysmal sweats (0-7)
8. Tactile disturbances (0-7)
9. Tremor (0-7)
10. Visual disturbances (0-7)

- Assessment takes <2 minutes to complete
- By adding up the scores of each 10 symptoms into a total, physicians can determine a severity range for patient's withdrawal syndrome
- Cumulative scoring:
 - $\leq 8-10$: mild withdrawal
 - 8-15: moderate withdrawal
 - ≥ 15 : severe withdrawal with impending possible delirium tremens

Cannabis Withdrawal

- **Mechanism:** heavy use can influence cannabinoid receptors
- 47% of individuals with regular or dependent cannabis use experience withdrawal symptoms



Cannabis Withdrawal

Withdrawal symptoms

- Insomnia or strange dreams
- Irritability
- Anxiety
- Low appetite
- Depression
- Nausea/vomiting
- Headaches

- **Onset:** days
- **Duration:** weeks or more
- **Treatment:** Over-the-counter remedies may help alleviate symptoms

Amphetamines and Stimulants Withdrawal

- Includes:
 - Methamphetamine
 - Cocaine
 - Rx amphetamines (Adderall, others)
 - Hallucinogenic amphetamines (MDMA, Molly, others)
- **Mechanism:** norepinephrine, dopamine, serotonin



Amphetamines and Stimulants Withdrawal

Withdrawal symptoms

- Fatigue
- Depression
- Anxiety
- Agitation
- Psychosis
- Muscle pain and spasms
- Cravings
- Anhedonia (reduced or inability to feel pleasure)

Amphetamines and Stimulants Withdrawal



- Onset: Hours to days
- Duration: 1-2 weeks or longer
- Treatments:
 - No standard of care
 - Benzodiazepines for agitation or psychosis
 - Antipsychotics and/or antidepressants

Antidepressants: SSRIs

- **Mechanism:**
 - Reduced serotonin in the central nervous system (CNS) as SSRI drug levels decrease
- **Onset:** within 7 days (often within 24 hours) of last dose
- **Treatment:**
 - Prevention is key!
 - Discontinuation via a slow taper over several weeks is recommended

Withdrawal Symptoms:

- Dizziness
- Headache
- Nausea
- Diarrhea
- Tremors
- Anxiety
- Agitation
- Confusion

Post-Acute Withdrawal Symptoms

- Delayed and persistent symptoms that occur after the initial withdrawal period is over
- Caused by chemical changes in the brain
- Start days to weeks after discontinuation of use and may last months or over a year
- Problems with mood, sleep, memory, motivation, attention, or other cognitive tasks
- Cravings!
- No medical treatment; exercise and social and mental health support can help

Detox Centers



- **Detoxification:** planned cessation of drug use in someone who is dependent
- Inpatient facilities help drug-dependent patients through acute withdrawal
- Provide medications and supportive care
- May provide psychological services
- Stay typically few days to a week or more

Addiction & Withdrawal Resources

- Washington Recovery Help Line 1-866-789-1511
 - www.washingtonrecoveryhelpline.com
- SAMSHA National Helpline 1-800-662-4357
 - www.samhsa.com
- Alcoholics/Narcotics Anonymous
- Primary-care providers
- Washington Poison Center!
 - Call 911 if patient is unconscious or not breathing

Addiction & Withdrawal Resources

- WA Department of Health Overdose Education & Naloxone Distribution:

www.doh.wa.gov/YouandYourFamily/DrugUserHealth/OverdoseandNaloxone

Thank you!!!

Interested in other trainings? Contact

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