

 OVERDOSE PREVENTION, HARM REDUCTION, & TREATMENT

AN EXPLORATION OF WITHDRAWAL

Marlo Murray, PharmD, CSPI

Certified Specialist in Poison Information

Washington Poison Center

Paul Cole, PharmD, CSPI

Certified Specialist in Poison Information

Washington Poison Center

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

Terms to know

- **Tolerance:** Reduced reaction to a drug following its repeated use
- **Dependence:** Physical requirement of the body for a drug. Without the drug, withdrawal symptoms occur
- **Withdrawal:** Clinical effects or symptoms that occur when a patient has a physical dependence on a drug or medication is stopped
- **Addiction:** Inability to stop use of a drug despite work, social, family, or personal consequences (also called Substance Use Disorder or SUD)
- **Taper:** Slowly decreasing or increasing a dosage over a period of time until the desired dosage is reached

Terms to know

- **Half-life:** The time it takes for the amount of a substance in the body to decrease by half
- **Detoxification:** planned cessation of substance use in someone who is dependent
- **Acute:** A one-time, single or short-term event
- **Chronic:** Long term or ongoing
- **Abstinence:** prolonged periods without drug or substance use
- **Recovery:** process of improved health, wellness and quality of life after abstinence from drugs

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

- Complex psychosocial situations
- Stigma
- Many withdrawal treatment options include substances that have their *own* potential for abuse/dependence/withdrawal

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)

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)
- Yawning
- Flu-like symptoms: runny nose/eyes

Opiates & Opioids Withdrawal

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



Opiates & Opioids



- Medication-assisted treatment
 - Methadone
 - Buprenorphine
 - Goal is to stabilize and sustain patient on new drug then may eventually taper off
 - May be combined with behavioral treatments

Opiates & Opioids

- **Kratom**
 - Plant from Southeast Asia
 - Contains compounds that are opioids
 - Legal and readily available in most of the US
 - Used and abused for effects similar to opioids



Opiates & Opioids



- **Kratom**
 - Withdrawal is similar to other opioids
 - Used by those struggling with substance use disorder as a substitute, or to avoid withdrawals

Opiates & Opioids



- **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

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!

Washington's Good Samaritan Law

Protects you from criminal penalties
for minor drug possession or having alcohol
under age 21 when you get help for someone
experiencing an overdose.

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

- Effects may 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

Benzodiazepines (BZD) Withdrawal

- Withdrawal treatment options
 - Switch to a long-acting benzodiazepine with a long duration of effect
 - Other medications (non-BZDs) are likely less effective at treating BZD withdrawal (antipsychotics, gabapentin, SSRIs, antihistamines)
 - 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

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
- 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
 - Can occur as blood alcohol level drops, 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 causes down-regulation of cannabinoid receptors
- 47% of individuals with regular or dependent cannabis use experience withdrawal symptoms



Cannabis Withdrawal

Withdrawal symptoms

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

- **Onset:** days
- **Duration:** weeks or more
- 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: several neurotransmitters, 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
- Withdrawal 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

Others

- **Gabapentin and pregabalin**

- Tolerance, psychological and physical dependence can occur
- Discontinue by tapering dose down over at least 1 week

Gabapentin and pregabalin withdrawal symptoms

- Confusion
- Irritability/anxiety/agitation
- Tachycardia (rapid heart rate)
- Diaphoresis (sweating)

- **Baclofen**

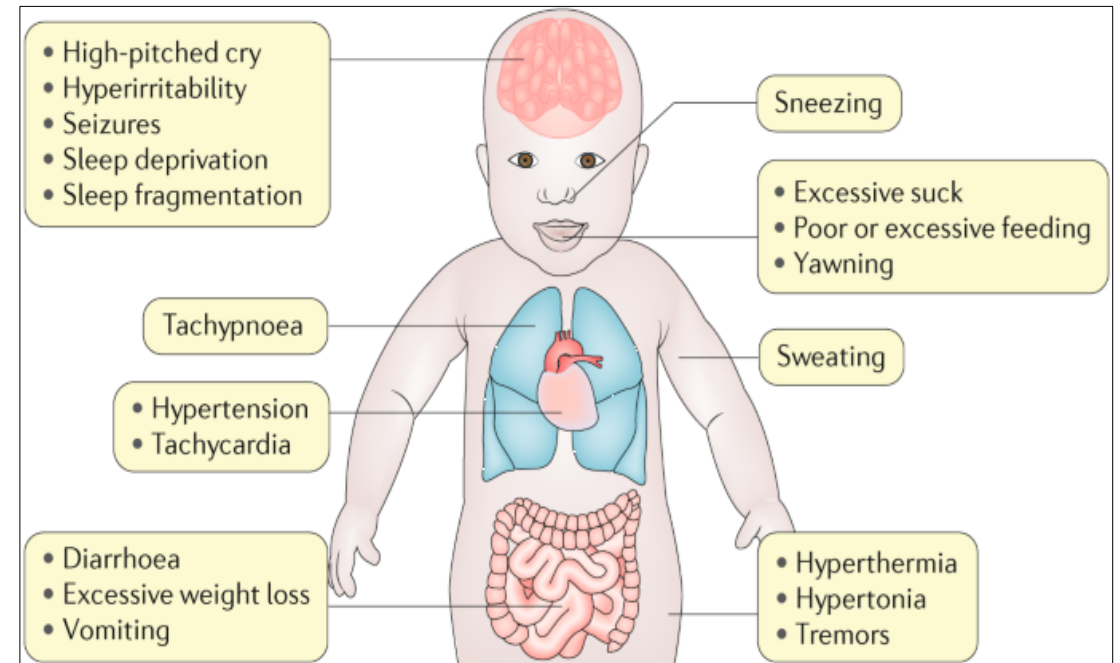
- Abrupt discontinuation of baclofen may cause fevers, altered mental status, muscle rigidity/spasticity, in severe cases organ failure, death
- Effects may be more extreme with baclofen pumps
 - Taper down oral baclofen dose over several weeks
 - Use caution when adjusting doses for baclofen pumps

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 treatment, but exercise and social and mental health support are important

Infant/Newborn Withdrawal

- Also called Neonatal Abstinence Syndrome (NAS)
- Mechanism: Maternal exposure to substances leads to exposure in utero; the baby's exposure stops abruptly at birth
- Can be life threatening
- May occur with or without low birth weight, birth defects or other effects of exposure to drugs in utero
- Can occur with many meds/drugs
 - Opioids
 - Kratom
 - Benzodiazepines
 - Others



Detox Centers



- 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
- Rapid detox

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!

Addiction & Withdrawal Resources

- WA Department of Health Overdose Education & Naloxone Distribution:

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



OVERDOSE PREVENTION, HARM REDUCTION, & TREATMENT

Thank you!!!



OVERDOSE PREVENTION, HARM REDUCTION, & TREATMENT

To request a Certificate of Attendance,
please email Meghan King at mking@wapc.org