Substance Abuse
Protracted Withdrawal

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Overview
1. Acute and Protracted Withdrawal
2. Withdrawal Potential
3. Recovery Reinforcers

Addiction
- Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations.
- It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Tolerance
- Higher or more frequent dosing to achieve the initial effects of the drug
- Neuroadaptation to continuously administered opioids
- Occurrence variable, not always linked with dependence
- Tolerance to non-analgesic effects beneficial
- Analgesic tolerance rarely the cause for dose escalation
- Dose escalation usually indicates disease change
- Tolerance does not imply addiction

Dependence
- Chronic medical condition
- Tolerance
- Withdrawal
- Lack of control
- Narrowing of behavior
- Continued use despite problems
- Need all or most of these symptoms to be considered drug dependent

Physical Dependence
- A state of neuroadaptation manifested by a drug class-specific withdrawal syndrome
- Produced by abrupt cessation, rapid dose reduction, decreasing bioavailability, or use of antagonist
- An expected occurrence in all individuals in the presence of continuous use of especially opioids for days or weeks.
Dependence, Addiction and Withdrawal

Physical Dependence or Addiction?
- Physical dependence is a normal physiologic response to the medical use of some prescriptions - especially opioids
- Addiction involves the non-medical use of medications
- Erroneous fear of addiction tragically promotes the under-treatment of pain

Substance Addiction Rating
- How easy to get hooked, how hard to stop?
  - Highest Addiction Potential
    - Nicotine, Ice (Meth), Cocaine (smoked or IV)
  - Mid-range Addiction Potential
    - Alcohol, Valium, Seconal, Heroin
  - Addictive
    - Caffeine, Marijuana, Ecstasy, Psychedelics

Acute Withdrawal
- ASAM - Acute withdrawal is usually referred to simply as “withdrawal.”
  - Withdrawal is “the onset of a predictable constellation of signs and symptoms following the abrupt discontinuation of, or rapid decrease in, dosage of a psychoactive substance.”
  - Such signs and symptoms are generally the opposite of the intoxication effects of the particular substance.
  - For example, pupils constrict during opioid intoxication and dilate during acute withdrawal.
  - These signs and symptoms begin within hours or days after last use of the substance and gradually resolve.
  - The length of time symptoms last depends on the particular substance used.

Acute Withdrawal Timeframes for Specific Substances

<table>
<thead>
<tr>
<th>Substance</th>
<th>Acute Withdrawal Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>5–7 days</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>3–4 weeks; 3–5 weeks with tapering (i.e., reducing dosage gradually)</td>
</tr>
<tr>
<td>Cannabis</td>
<td>5 days</td>
</tr>
<tr>
<td>Nicotine</td>
<td>2–4 weeks</td>
</tr>
<tr>
<td>Opioids</td>
<td>4–10 days (methadone withdrawal may last 14–21 days)</td>
</tr>
<tr>
<td>Stimulants (e.g., amphetamines, methamphetamine, cocaine)</td>
<td>1–2 weeks</td>
</tr>
</tbody>
</table>

Theory of Protracted Withdrawal
- Koob and colleagues have shown that brain adapts to repeated use of DA-releasing reinforcer by “turning down” the reinforcement/reward pathway so that when the addict abstains, “life is just less fun” unless they use their drug of choice.
- May be the reason for stress-induced relapse and dysphoria of early abstinence

Protracted Withdrawal
- Strictly Defined: The presence of substance-specific signs and symptoms common to acute withdrawal but persisting beyond the generally expected acute withdrawal timeframes
- Broader Definition: includes the experiencing of the above symptoms and of non-substance-specific signs and symptoms that persist, evolve, or appear well past the expected timeframe for acute withdrawal.
- Each psychoactive substance class has different effects on the brain.
Other Terms

- Chronic withdrawal
- Extended withdrawal
- Late withdrawal
- Long-term withdrawal
- Persistent postuse symptoms
- Postacute withdrawal syndrome (PAWS)
- Postuse syndrome
- Protracted abstinence
- Sobriety-based symptoms
- Subacute withdrawal

Symptoms of Protracted Withdrawal

- Anxiety
- Sleep difficulties
- Problems with short-term memory
- Persistent fatigue; irritability
- Difficulty focusing on tasks
- Difficulty concentrating and making decisions
- Alcohol or drug cravings
- Impaired executive control
- Anhedonia
- Dysphoria or depression
- Unexplained physical complaints
- Reduced interest in sex

Protracted Withdrawal Symptoms

- Chronic substance use causes molecular, cellular, and neurocircuitry changes to the brain that affect emotions and behavior and that persist after acute withdrawal has ended.
- Adaptive changes in the central nervous system may lead to affective changes that persist for many weeks or longer beyond acute withdrawal.
- Repeated use of a substance causes the brain to respond more readily to its effects but less readily to naturally rewarding activities such as listening to music - a state of decreased ability to experience pleasure known as anhedonia.

Protracted Withdrawal

- Abstinence syndrome
  - Anxiety
  - Muscle twitching
  - Low mood
  - Sweating
  - Headache
  - Derealization
  - Rebound insomnia
  - Especially with short-acting benzodiazepines

Commonly Misused Rx Drugs

- Opiates: pain-killers
  - i.e. Vicodin, Oxycontin, Tylenol Codeine
- CNS Depressants (Sedatives/Tranquilizers)
  - i.e. Xanax, Ativan, Valium, Soma
- Stimulants: ADHD, weight loss
  - i.e. Aderall, Ritalin, Concerta, Dexedrine, Fastin (OTC Diet Pill)
Alcohol withdrawal syndrome

- Onset: 6-24 hours after last drink
- Duration: 2-10 days
- Symptoms:
  - Anxiety
  - Excess perspiration
  - Tremors
  - Dehydration
  - Increased heart rate, blood pressure
  - Insomnia
  - Nausea and vomiting
  - Diarrhea

Sleep Abnormalities - Alcohol

- Anecdotal literature and case studies going back several decades suggest that signs and symptoms may last 2 years or longer after the last use of alcohol.
- A review of seven sleep studies using polysomnograph recordings of the brain while people slept found evidence that sleep abnormalities can persist for 1 to 3 years after stopping alcohol consumption.
- These abnormalities include difficulty falling asleep, decreased total sleep time, and sleep apnea.

Benzodiazepine withdrawal syndrome

- Short-acting benzodiazepines (insomnia):
  - Onset 1-2 days after last dose
  - Duration 2-4 weeks or longer
- Long-acting benzodiazepines (anxiety):
  - Onset 2-7 days after last dose
  - Duration 2-8 weeks or longer
- The protracted withdrawal can be minimized in intensity and severity by a slow gradual reduction in dosage

Benzodiazepines

- Benzodiazepine protracted withdrawal may be difficult to diagnose because of difficulty distinguishing it from symptom rebound or symptom reemergence
- Protracted withdrawal symptoms typically wax and wane in intensity and are new to the client (i.e., they do not indicate symptom reemergence).
- Clients also may have no symptoms for a time after stopping benzodiazepine use and then become extremely anxious.
- Psychological symptoms can mimic disorders such as agitated depression, generalized anxiety, panic, or obsessive-compulsive disorders, and schizophrenia. Fluctuating protracted withdrawal symptoms may last for months but gradually subside with prolonged abstinence.

Opioid withdrawal syndrome

- Symptoms:
  - Nausea and vomiting
  - Anxiety
  - Insomnia
  - Hot and cold flushes
  - Perspiration
  - Muscle cramps
  - Watery discharge from eyes and nose
  - Diarrhea

Stimulant withdrawal syndrome

- Onset: within 24 hours of last use
- Duration: 3-5 days
- Symptoms:
  - Agitation and irritability
  - Depression
  - Increased sleeping and appetite
  - Muscle aches
### Inhalant Withdrawal Syndrome
- **Onset:** anywhere from a few hours to a few days after ceasing use
- **Duration:** anywhere from 2 days to 2 weeks

### Withdrawal Management for Cannabis Dependence
Cannabis withdrawal syndrome is poorly understood:
- Typically mild, yet difficulty coping with
- Symptoms last for 1-2 weeks
- Sleep difficulties and strange dreams can persist at least 45 days into abstinence (the longest duration of the studies)

### CANNABINOIDS
- 10 hours after use
  - Tremor of the tongue and extremities
  - Insomnia
  - Sweats
  - Lateral gaze nystagmus (rhythmic oscillation of the eyeball on lateral gaze)
  - Exaggerated deep tendon reflexes

### Helping Clients Through Protracted Withdrawal
- Clients affected by anhedonia and other symptoms of protracted withdrawal may want to alleviate those symptoms by returning to substance use at a time when they may have a weakened ability to resist such impulses.
- Treatment providers can improve their clients’ chances for long-term recovery by educating clients about protracted withdrawal, offering support and understanding, monitoring them regularly, and intervening early with clients who seem headed for relapse.

### Educate clients about protracted withdrawal and help them develop realistic attitudes toward recovery.
- Remind clients that recovery is a process. Help clients understand that it is normal to feel not fully recovered within the first weeks and months of abstinence.
- Tell them about possible protracted withdrawal symptoms and reassure them that these symptoms will not last forever and can be managed.
- Advise clients on how to reduce or cope with symptoms and encourage them to focus on incremental improvements.
- Tell clients it takes time to undo the damage from substance use but in many cases, with long-term abstinence, substance-induced brain changes reverse.
- Celebrate each accomplishment - learning a new coping skill - and help clients not become discouraged if symptoms recur.

### Reassess During Recovery
The symptoms of protracted withdrawal can be similar to those of TBI and CODs.
- Assess and reassess clients for suicide as recovery proceeds, including for depression and suicidal tendencies. (TIP 42, TIP 48 and TIP 50 provide more information on CODs and suicide.
- Discuss sleep problems - determine if possible sleep problems stem from protracted withdrawal or are the result of other causes: e.g. sleep habits retained from a substance-using lifestyle, CODs, relapse to substance use, stress, or side effects of medication (including medication to treat SUDs).
- Educate clients about good sleep habits: adopting a regular sleep routine, exercising early in the day, minimizing caffeine intake, eating well, and avoiding late afternoon naps. Use pharmacological treatments with caution to avoid use problems.
## Recovery Advice

- Advise clients to be active. Encourage engagement in physical and mental exercises, which improve sleep, promote positive emotional states, reduce stress and nervousness.
- Help clients avoid triggers, and distract clients' attention from symptoms.
- Advise Self Care and Patience - Clients in early recovery may try to “make up for lost time” by overbooking and generally trying to do too much, increasing overall stress levels and possibly exacerbating symptoms.
- Prescribe medications as needed to control symptoms past the acute withdrawal stage – discuss the use of medications, such as Acamprosate, might relieve some protracted withdrawal symptoms.

## REFERENCES

- Substance Abuse Treatment Advisory, July 2010, Volume 9, Issue 1
- World Health Organization