

PROTRACTED WITHDRAWAL

Most clients in treatment for substance use disorders (SUDs) do not immediately feel better after stopping their substance use. In a pattern unique to each client, symptoms related to substance abuse may be felt for weeks, months, and sometimes years. Clients may be affected by less intense versions of the acute signs and symptoms of withdrawal as well as by other conditions such as impaired ability to check impulses, negative emotional states, sleep disturbances, and cravings. These symptoms may lead clients to seek relief by returning to substance use, feeding into the pattern of repeated relapse and return to treatment.^{1, 2} SUD treatment providers can help clients avoid this cycle by helping them recognize and manage symptoms.

Some clients in recovery also experience symptoms from co-occurring substance use and mental disorders. The SUD treatment provider's challenge is to determine which of a client's abstinence symptoms are substance-use related and will resolve over time and which indicate a possible co-occurring disorder (COD) that calls for a thorough assessment by a mental health provider and concurrent care. Treatment Improvement Protocol (TIP) 42: *Substance Abuse Treatment for Persons With Co-Occurring Disorders* provides more information on CODs and their treatment.³

This *Advisory* differentiates acute withdrawal from protracted withdrawal, provides an overview of protracted withdrawal signs and symptoms, and offers suggestions on how to help clients manage protracted withdrawal in recovery.

What is acute withdrawal?

Acute withdrawal is usually referred to simply as "withdrawal." The American Society of Addiction Medicine defines withdrawal as "the onset of a predictable constellation of signs and symptoms following the abrupt discontinuation of, or rapid decrease in, dosage of a psychoactive substance."⁴ Such signs and symptoms are generally the opposite of the intoxication effects of the particular substance.⁵ 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. Exhibit 1 lists approximate timeframes for acute withdrawal from several substances.

Exhibit 1. Acute Withdrawal Timeframes for Specific Substances

Substance	Acute Withdrawal Timeframe
Alcohol ^{6, 7}	5–7 days
Benzodiazepines ^{8, 9}	1–4 weeks; 3–5 weeks with tapering (i.e., reducing dosage gradually)
Cannabis ¹⁰	5 days
Nicotine ¹¹	2–4 weeks
Opioids ¹²	4–10 days (methadone withdrawal may last 14–21 days)
Stimulants (e.g., amphetamines, methamphetamine, cocaine) ¹³	1–2 weeks

What is protracted withdrawal?

Protracted withdrawal, strictly defined, is the presence of substance-specific signs and symptoms common to acute withdrawal but persisting beyond the generally expected acute withdrawal timeframes noted in Exhibit 1. A broader definition of protracted withdrawal, and the one used in this *Advisory*, 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. Exhibit 2 lists other terms sometimes used for protracted withdrawal.

Exhibit 2. Synonyms for Protracted Withdrawal

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

Despite clinical observation and clients' reports of symptoms experienced past the acute withdrawal stage, the research on protracted withdrawal (particularly for substances other than alcohol) is limited, and no consensus on the term or definition exists. These reasons have precluded the *Diagnostic and Statistical Manual of Mental Disorders* from including a protracted withdrawal diagnosis for any psychoactive substance.⁶ For these reasons also, this *Advisory* does not provide timeframes for protracted withdrawal as is done for acute withdrawal in Exhibit 1.

How do protracted withdrawal symptoms develop?

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.^{14, 15, 16, 17} Adaptive changes in the central nervous system may lead to affective changes that persist for many weeks or longer beyond acute withdrawal.¹⁸ For example, 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. This state, in which a person's ability to experience pleasure is decreased, is called *anhedonia*. Pozzi and colleagues examined anhedonia in individuals who had been abstinent from alcohol, opioids, and/or other drugs for a period and who had no identified CODs.¹⁹ Their study examined whether anhedonia may be linked to psychosocial factors in the lives of people recovering from SUDs. They conclude that anhedonia appeared to be a symptom of protracted withdrawal that was unrelated to other clinical and psychosocial features. Martinotti and colleagues found that signs and symptoms, including anhedonia, lasted the duration of a year-long study of people recovering from alcohol use disorders.²⁰

A variety of other symptoms have been attributed to protracted withdrawal, including anxiety, sleep difficulties, problems with short-term memory, persistent fatigue, difficulty concentrating and making decisions, alcohol or drug cravings, and impaired executive control (e.g., impulse control, solving problems).

Are protracted withdrawal symptoms the same for all substances?

No. They are similar but not identical. Each psychoactive substance class has different effects on the brain.

Protracted withdrawal from alcohol has been well documented. Common protracted withdrawal symptoms include anxiety, hostility, irritability, depression, mood

ADVISORY

instability, fatigue, insomnia, difficulties concentrating and thinking, reduced interest in sex, and unexplained physical complaints especially of pain. 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.²¹ These abnormalities include difficulty falling asleep, decreased total sleep time, and sleep apnea.

Research on drug-specific protracted withdrawal signs and symptoms is scarce but indicates the following:

- **Opioids.** Symptoms such as anxiety, depression, and sleep disturbances can last for weeks or months following withdrawal from opioids.²² Other possible symptoms include fatigue, dysphoria (i.e., feeling down or emotionally blunted), and irritability.¹² A small National Institutes of Health study found that subjects who had been abstinent from opioids for a prolonged period showed decreased ability to focus on a task compared with subjects who had never used opioids.²³ People in recovery from heroin dependence also show deficits in executive control functions that may persist for months beyond the period of acute withdrawal.²⁴
- **Methamphetamine.** A 2007 review noted that studies have shown that deficits in executive control functions resulting from amphetamine use also persist well into recovery from methamphetamine dependence.²⁵
- **Cocaine.** Fox and colleagues examined emotional regulation issues and problems with impulse control in newly abstinent individuals dependent on cocaine.²⁶ Significant improvement in several aspects of emotional regulation (e.g., understanding and managing emotions, ability to develop emotional coping strategies) was seen after 4 weeks of abstinence. However, impulse control had *not* improved after 4 weeks of abstinence.

- **Marijuana.** A review of 19 studies of marijuana withdrawal found that sleep difficulties and strange dreams persisted at least 45 days into abstinence (the longest duration of the studies).²⁷
- **Benzodiazepines.** Benzodiazepine protracted withdrawal may be difficult to diagnose because of difficulty distinguishing it from *symptom rebound* or *symptom reemergence* (Exhibit 3).²⁸ 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.

Exhibit 3. Symptom Rebound and Symptom Reemergence

Symptom rebound, the most common aftereffect of prolonged benzodiazepine use, is the intensified return of acute withdrawal signs and symptoms. These acute symptoms are typically opposite the effects of the drug (e.g., anxiety, insomnia, restlessness) and tend to abate in a few weeks.²⁹

Symptom reemergence is the return of symptoms (e.g., anxiety, muscle tension, insomnia) at the same level as those experienced before benzodiazepines were prescribed or taken. These symptoms do *not* abate with time. Because these symptoms were present before the substance use began, they suggest the presence of an underlying pathology needing treatment.³⁰

Do all clients experience protracted withdrawal?

No. Some clients experience no symptoms after the acute withdrawal stage, whereas others have lingering symptoms. Still others experience an initial clearing of symptoms for the first month or two of abstinence and then develop unpleasant symptoms again. The intensity of symptoms also differs among clients.

How can providers help 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 (Exhibit 4) 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** (e.g., learning a new coping skill) and help clients not become discouraged if symptoms recur. Repeat encouragements at each meeting, especially with

Exhibit 4. Possible Symptoms of Protracted Withdrawal

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

clients affected by memory and concentration impairments.

- **Assess for CODs.** The symptoms of protracted withdrawal can be similar to those of traumatic brain injury (TBI) and CODs. Carefully assess and reassess clients as recovery proceeds, including for depression and suicidal tendencies. TIP 42,³ TIP 48: *Managing Depressive Symptoms in Substance Abuse Clients During Early Recovery*,³¹ and TIP 50: *Addressing Suicidal Thoughts and Behaviors in Substance Abuse Treatment*³² provide more information on CODs and suicide. An *Advisory* in development will provide information on assessing and addressing TBI in recovery.³³ Appropriate treatment of a COD positively affects the course of treatment.³⁴
- **Ask about sleep problems.** Make a differential diagnosis to determine whether a client's sleep problems likely stem from protracted withdrawal or are the result of other causes. Such causes include poor sleep habits retained from a substance-using lifestyle, CODs, relapse to substance use, stress, or

ADVISORY

side effects of medication (including medication to treat SUDs). Educate clients about good sleep habits: adopting a regular sleep routine (going to bed and getting up at the same times), exercising early in the day, minimizing caffeine intake, eating well, and avoiding late afternoon naps. Use pharmacological treatments with caution to avoid use problems.

The Substance Abuse and Mental Health Services Administration's (SAMHSA's) Center for Substance Abuse Treatment (CSAT) is developing a *Substance Abuse in Brief Fact Sheet* on sleep problems that will provide more information.³⁵

- **Advise clients to be active.** Encourage clients to engage 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. Assist clients in adopting habits that help them cope with memory and thinking problems (e.g., making to-do lists, establishing daily routines).
- **Advise clients to be patient.** Clients in early recovery may try to "make up for lost time" by overbooking and generally trying to do too much, increasing their overall stress levels and possibly exacerbating symptoms. Tell clients that they are doing enough by focusing on their recovery and regaining their health.
- **Prescribe medications as needed to control symptoms past the acute withdrawal stage.** Inform clients recovering from alcohol addiction that treatment medications, such as acamprosate, might relieve some protracted withdrawal symptoms. Although acamprosate's mechanism of action is not well understood, it may reduce uncomfortable symptoms such as anxiety and sleep disturbances that clients feel after they have stopped drinking. SAMHSA's CSAT *Advisory* on acamprosate provides more information.³⁶ Consider methadone or buprenorphine replacement treatment for clients who find that protracted opioid withdrawal symptoms

are too powerful and for whom the risk of relapse is high.³⁷

- **Encourage clients to join mutual support groups.** Tell clients that participation in mutual support groups such as Alcoholics Anonymous or Women in Sobriety is associated with long periods of recovery. Make clients aware of population-specific support groups (e.g., adolescents- or women-only groups). Direct clients in medicated-assisted treatment to support groups that accept the use of prescribed medications for substance abuse treatment. Tell clients that they may need to visit several groups over several weeks to find groups with which they feel comfortable. SAMHSA's CSAT *Substance Abuse in Brief Fact Sheet* on mutual support groups provides more information.³⁸
- **Include interventions that help clients strengthen executive control functions.** Provide interventions such as cognitive-behavioral therapy to help clients manage problems with impulse control, solve problems, and make decisions.³⁹
- **Monitor clients for symptoms during continuing care.** Provide clients with opportunities to obtain professional guidance on such issues as lapses and relapses, stress, triggers, and activities to maintain abstinence. Monitoring can be through periodic office visits or by telephone or email. Arrange for transition to a case manager as needed.⁴⁰

SAMHSA Resources

Several publications are available free of charge from SAMHSA's Health Information Network. The resources listed on page 6 can be ordered at <http://www.samhsa.gov/shin>. Or, please call 1-877-SAMHSA-7 (1-877-726-4727). The publications also can be downloaded from the Knowledge Application Program Web site at <http://www.kap.samhsa.gov>.

Resources for professionals

Substance Abuse Treatment Advisory, Acamprosate: A New Medication for Alcohol Use Disorders. (2005). HHS Publication No. (SMA) 05-4114.

TIP 42: *Substance Abuse Treatment for Persons With Co-Occurring Disorders.* (2005). HHS Publication No. (SMA) 05-3992.

TIP 43: *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs.* (2005). HHS Publication No. (SMA) 05-4048.

TIP 45: *Detoxification and Substance Abuse Treatment.* (2006). HHS Publication No. (SMA) 06-4131.

TIP 48: *Managing Depressive Symptoms in Substance Abuse Clients During Early Recovery.* (2008). HHS Publication No. (SMA) 08-4353.

TIP 50: *Addressing Suicidal Thoughts and Behaviors in Substance Abuse Treatment.* (2009). HHS Publication No. (SMA) 09-4381.

Resources for clients

The Facts About Buprenorphine for Treatment of Opioid Addiction. (2009). HHS Publication No. (SMA) 09-4442.

The Facts About Naltrexone for Treatment of Opioid Addiction. (2009). HHS Publication No. (SMA) 09-4444.

Medication-Assisted Treatment for Opioid Addiction: Facts for Families and Friends. (2009). HHS Publication No. (SMA) 09-4443.

What Is Substance Abuse Treatment? A Booklet for Families. (2004). HHS Publication No. (SMA) 08-4126.

Notes

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