

Withdrawal from Alcohol, Cocaine, and Heroin

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Up to 40 percent of hospital admissions are related to problems of substance abuse.¹ Patients who abuse alcohol or drugs may be admitted to the hospital for trauma or another medical problem, then develop an acute withdrawal syndrome while inpatient. Recognition and treatment of the appropriate withdrawal syndrome is important to prevent excess mortality or prolonged hospitalization due to complications.

Alcohol and Sedative-Hypnotic Medications

Sedative-hypnotic drugs include alcohol, benzodiazepines, barbiturates, and other sleeping pills. This type of prescription medication has significant potential for abuse. It is unusual to see patients who are solely abusing prescription medication. The majority of sedative-hypnotic abusers take one or more benzodiazepines and ethanol, along with barbiturates and other sleeping pills.

Signs of Withdrawal – The withdrawal syndrome manifests with the same signs and symptoms for alcohol or any of the other sedative-hypnotic medications. This consists of escalating autonomic instability that usually begins within 48 hours of the last drink, although many of the benzodiazepines have long-acting metabolites, so the patient may not show signs of withdrawal for 7 to 10 days after stopping all drugs. The signs of the withdrawal syndrome are presented in Table 1; progression to severe withdrawal carries a significant mortality, so early recognition and treatment is essential.

Treatment of mild to moderate withdrawal — Treatment is identical for withdrawal from all sedative-hypnotics, including barbiturates, sleeping pills, benzodiazepines, and alcohol. All drugs in these categories exhibit cross-dependence.

The first step is to objectively determine an approximate level of drug to which the patient is tolerant; patients tend to over- or underestimate the amount of alcohol or other drug they have been taking. Very precise instruments for the measurement of tolerance exist, but often are not practical and in many cases are not necessary.

While any medication with cross-dependence can be used, a scheme for using phenobarbital follows:²

- An initial dose is given, usually 60 to 90 mg of phenobarbital (or an equivalent dose of another sedative-hypnotic such as diazepam or clonazepam, see Table 2), and the patient is monitored for at least 6 to 8 hours.

- The withdrawal drug is repeated at hourly or two-hour intervals as indicated by the signs of withdrawal the patient is exhibiting.

- After 8 hours, an approximation can be made of the total dose the patient will require for a 24-hour period. It is better to err on the side of slightly over- rather than undermedicating.

Tapering is started from the dose calculated above. Reducing the dose by 10 percent of the initial dose each day provides a comfortable taper, especially if the patient has coexisting medical conditions. The taper can be accomplished more rapidly if these conditions do not exist.

Long-acting medications decrease the severity of withdrawal symptoms; phenobarbital may be chosen in preference to other sedatives since it has a longer half-life than diazepam, patients rarely achieve a "high" from phenobarbital as they do from the other drugs, and it is available in multiple dosage forms. The dose of phenobarbital can be given in a constant volume of liquid for each dose so the patient is not aware of the amount being decreased each day ("blind taper").

Anticonvulsant agents that do not show cross-dependence with sedative-hypnotics (carbamazepine, valproate) have been used successfully in the treatment of mild sedative-hypnotic withdrawal.³ They are given at full anticonvulsant doses for several weeks. These medications have not been studied for use in severe withdrawal.

Treatment of advanced withdrawal ("Delirium Tremens")— Advanced sedative-hypnotic withdrawal (e.g., markedly abnormal vital signs, delirium) should be treated rapidly and with sufficiently large doses of medication to suppress the withdrawal. Medications with a rapid onset of action should be used and may be given intravenously for immediate effect. Lorazepam and diazepam are good choices since they have a rapid onset of action when given intravenously, although they have a shorter duration of action than when given orally since first-pass liver metabolism is bypassed. For example, give lorazepam 1-4 mg intravenously every 10-30 minutes until the patient's agitation or delirium improves so that the patient is calm but awake, and

the heart rate decreases to around 100 beats/minute.

After stabilization with rapid-acting medications, the patient can be switched to an equivalent dose of a long-acting medication such as phenobarbital, oral diazepam, or clonazepam. The awake patient will not undergo significant respiratory depression from the withdrawal medication; at times very large doses are required (up to 700 mg of phenobarbital per day).

Cocaine and Other Stimulants

Stimulants are drugs that stimulate the central nervous system (CNS) to produce increased psychomotor activity. Amphetamines and cocaine are the most prevalent stimulants abused. Cocaine is a short-acting local anesthetic with marked stimulant effects.

Signs of Withdrawal— An abstinence syndrome can occur with chronic stimulant use that is characterized by symptoms that are more subtle and complex than those previously associated with drug withdrawal. The "crash," or drastic reduction in mood and energy, starts 15 to 30 minutes after cessation of a stimulant binge. Addicts experience craving, depression, anxiety, and paranoia. The craving for stimulants decreases over one to four hours and is replaced by a craving for sleep and rejection of further stimulant use. Hypersomnolence lasts eight hours to four days. Sleep is punctuated by brief awakenings during which the addict experiences hyperphagia ("the munchies"). Then begins a protracted dysphoric syndrome in which the addict experiences anhedonia, boredom, anxiety, generalized malaise, problems with memory and concentration, and occasional suicidal ideation. This induces severe craving that may lead to resumption of stimulant use and a vicious cycle of recurrent binges. Intermittent conditioned craving can last months to years after the last stimulant use, and is gradually extinguished over time. The severity and duration of withdrawal depends upon the intensity of the preceding months of chronic abuse and the presence of predisposing psychiatric disorders, which amplify withdrawal symptoms.

If marked depression persists longer than one week after withdrawal, the patient should be evaluated carefully to determine if he or she is "self-medicating" an underlying depression, which then should be treated with a specific antidepressant.

Treatment— Abrupt discontinuation of stimulants does not cause gross physiologic sequelae. Thus,

they generally are not tapered or replaced with a cross-tolerant drug during medically supervised withdrawal. Propranolol may be effective in reducing severe cocaine withdrawal symptoms,⁴ but may aggravate cocaine-induced hypertension or coronary artery vasoconstriction.⁵

Heroin and Other Opioids

Opioids are used therapeutically as analgesics, and heroin is an opioid with significant potential for abuse.

Signs of Withdrawal— Opioid-dependent patients experience withdrawal symptoms when the drug is discontinued. See Table 3 for a list of opioid withdrawal signs. Abrupt withdrawal usually causes physical effects no worse than a bad case of influenza. However, this form of therapy is not justifiable because of the extreme anxiety experienced by opioid users upon sudden drug cessation.

Treatment— Virtually any opioid can be administered to relieve acute withdrawal symptoms. The effects of short-acting medications (e.g., morphine, hydromorphone) can be controlled precisely but require frequent assessment and dose adjustment, and patients may experience severe withdrawal symptoms toward the end of the dosing period. Short-acting medications are most appropriately used in intensive care units or in other situations when the patient's condition is likely to change rapidly and the patient can be closely monitored. Long-acting medications are more convenient for medical and nursing staff, produce less severe withdrawal symptoms themselves (if any symptoms are seen), but the withdrawal symptoms may last for long periods of time; they are most appropriately used when the patient is medically stable (other than having opioid withdrawal).

Short-acting opioids— Short-acting opioids such as morphine, hydromorphone, or fentanyl are most often used in settings where the patient can be closely monitored, such as an intensive care unit. This allows for rapid titration of parenteral medication with short onset latency and duration of action. The opioid can be given as an intravenous bolus or continuous infusion. The severity of 10 symptoms (see Table 3) is graded on a scale of 0 to 2 points: 0 points if the symptom is absent; 1 point if the symptom is present; and 2 points if the symptom is severe. Determine the total score for all 10 symptoms, then administer morphine sulfate (or another short-acting opioid) intravenously with frequent assessments until the withdrawal score is

reduced to 0-5 points.⁶ The dose of parenteral opioid can be increased rapidly in 1-mg increments every 5 minutes to reduce withdrawal signs. Once the patient's withdrawal is stabilized, reduce the total daily dose of morphine by 10% per day over 10 days. If the patient is to be converted to oral medication, give oral methadone in fixed volume at a morphine-methadone conversion of 1:10 (for example, if the patient is receiving morphine 3 mg/hr, then give methadone 30 mg/day or 15 mg q12h). Then follow the instructions for tapering methadone as described below.

Methadone— Methadone is frequently used to treat acute withdrawal symptoms from illicit opioids. Current federal regulations restrict the use of methadone for treatment of opioid addiction.⁷ Methadone may be used by a private practice physician for temporary maintenance or detoxification when an addicted patient is admitted to a hospital for an illness other than opioid addiction. It may also be used by a private practitioner in an outpatient setting when administered daily for a maximum of three days while a patient awaits admission into a licensed methadone treatment program.⁸ A Drug Enforcement Administration (DEA) license to prescribe Schedule II medications is required.

A method of titrating the amount of methadone based upon symptoms has been used extensively to titrate methadone for opioid withdrawal, without causing over-sedation or severe patient discomfort.²

- The severity of 10 symptoms (see Table 3) is graded on a scale of 0 to 2 points:
 - 0 points if the symptom is absent;
 - 1 point if the symptom is present;
 - 2 points if the symptom is severe.
- The total score for all 10 symptoms is determined; each point is equivalent to a requirement of 1 mg of methadone, although there is no need to give any methadone for a score of less than 5 points, since such a low score indicates only mild withdrawal.
- The patient should be evaluated and the symptom score totaled every 6 hours for the first 24 hours.
- After 24 hours, the total dose of methadone that has been administered is computed; this dose is approximately equivalent to the dose of opioid the individual was taking. After being stabilized

on this dose of methadone, the patient can be withdrawn by gradually reducing the dose.

- The total daily intake should be reduced by approximately 10 percent per day. The duration of action of methadone allows it to be given once daily as a single dose. Patients do not experience a "rush," or initial euphoria, with methadone administration. The calculated withdrawal schedule should not be altered unless the patient shows objective signs of worsening. The patient is blinded to the dose by giving methadone as an elixir mixed with orange juice. The patient receives the same volume of liquid each day, but the amount of juice is increased as the methadone dose is reduced. This helps alleviate anxiety the patient might have as the dose is decreased.

Frequently, patients receiving methadone require analgesic medications for coexisting medical problems, acute trauma, or post-operative pain. Attempts should be made to control the pain through the use of non-narcotic analgesics in most cases. If this is not possible, the dose of methadone that the patient is receiving should be used as a baseline, with additional narcotic analgesics added in standard therapeutic doses to control the pain. Pentazocine (Talwin), nalbuphine (Nubain), and butorphanol (Stadol) should **not** be administered to any patient taking pure agonists such as methadone because these drugs have antagonist properties and can precipitate an immediate withdrawal.^{9,10}

If a methadone maintenance client is hospitalized, such as for a traumatic injury or medical illness, the maintenance dose should be continued throughout hospitalization. The hospital physician should contact the methadone maintenance program to verify the client's current dose and arrange for dosing to resume after discharge. Acutely ill or injured hospital patients often experience pain; methadone maintenance clients experience the same pain despite being on methadone, since methadone reaches steady state levels in the body and does not provide additional analgesia. Methadone maintenance patients with acute pain should be given pain medications (whether narcotic or nonnarcotic) as though they were not on methadone. The only exception, as previously mentioned, is that pentazocine (Talwin), nalbuphine (Nubain), and butorphanol (Stadol) should **not** be administered because these drugs have antagonist properties and can precipitate an immediate withdrawal.^{9,10}

Table 1. Sedative-Hypnotic Withdrawal Syndrome

Sign	Mild Withdrawal	Severe Withdrawal
Blood Pressure	Slight increase (esp. systolic)	Significant hypertension or hypotension
Heart rate	Slight increase	Significant increase (>120 bpm)
Temperature	Slight increase (up to 101.5 degrees Fahrenheit)	Significant increase (>101.5 degrees Fahrenheit)
Respiratory rate	Slight increase (up to 20/min)	Significant increase (>20/min)
Orientation	Minimally disoriented	Disoriented
Consciousness	Agitated	Delirious
Hallucinations	None	Visual, possibly auditory
Tremors	Fine tremors of hands or tongue	Gross tremors of all extremities
Seizures	Possible	Unlikely

Table 2. Sedative-Hypnotic Equivalent Doses

<u>Medication</u>	Equivalent Oral Dose (mg)	Usual Dose Interval (hours)
Alprazolam (Xanax)	1	4-6
Butalbital (Fiorinal, Fioricet)	100	4
Chloral hydrate (Noctec)	500	8
Chlordiazepoxide (Librium)	25	6
Clonazepam (Klonopin)	2	8
Clorazepate (Tranxene)	7.5	8
Ethchlorvynol (Placidyl)	500	6
Diazepam (Valium)	10	6-8
Flurazepam (Dalmane)	15	12
Glutethimide (Doriden)	250	8
Lorazepam (Ativan)	2	6-8
Meprobamate (Miltown)	400	6
Oxazepam (Serax)	10	6
Pentobarbital (Nembutal)	100	4
Phenobarbital (Luminal)	30	8-12
Secobarbital (Seconal)	100	4
Temazepam (Restoril)	15	6
Triazolam (Halcion)	0.25	2

From Drug Facts and Comparisons¹⁵, Physician's Desk Reference¹⁶, and Gilman et al.¹⁷

Table 3. Opioid Withdrawal Signs

Pupil dilation
Lacrimation (watery eyes)
Rhinorrhea (runny nose)
Piloerection (gooseflesh, body hair stands up)
Nausea, vomiting
Diarrhea, abdominal cramps
Chills, hot flashes
Myalgias (muscle aches), arthralgias (joint aches), muscle cramps, twitching
Yawning
Restlessness, irritability, insomnia

Clonidine and other medications — Clonidine, an alpha-2 adrenergic receptor agonist, reduces catecholamine release in the sympathetic nervous system and thereby effectively decreases withdrawal symptoms in patients taking low doses of opioids.¹¹⁻¹³ Clonidine doses as high as 1.2 mg/day in divided doses have been used to manage opioid withdrawal, although side effects with higher doses, including orthostatic hypotension, sedation, dry mouth, and constipation, may be significant. Clonidine also can be used to facilitate methadone withdrawal when the methadone dose is tapered below 15 mg.¹⁴ It is important to monitor for hypotension during clonidine therapy and then to gradually taper clonidine to avoid a hypertensive rebound. A clonidine patch is effective for mild withdrawal symptoms and can be left on the skin for seven days.

Additional medications may be given for relief of other acute symptoms of opioid withdrawal: muscle relaxants reduce spasms and twitching; nonsteroidal anti-inflammatory drugs treat aches; antiemetics are used for nausea; an antidiarrheal agent such as bismuth subsalicylate may be useful; and a sleeping medication that has low abuse potential (such as trazodone) will help insomnia.

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