

# Drug Withdrawal

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## Specific Learning Objectives

### Knowledge

Subinterns should be able to describe and define:

- a) History findings that identify patients admitted for reasons other than detoxification at risk for withdrawal from alcohol or other substances of abuse
- b) The symptoms and physical exam findings of different stages of alcohol withdrawal
- c) The timing of and risk factors for alcohol withdrawal seizures and delirium tremens (DTs)
- d) Non-pharmacologic treatment of alcohol withdrawal, including modifying environmental stimuli
- e) The need for early, aggressive treatment of withdrawal to prevent the development of complications
- f) The indications for short-term nicotine replacement therapy in medical inpatients unable leave the ward to smoke but uninterested in smoking cessation
- g) The impact on hospital length-of-stay and discharge planning in initiating methadone therapy for narcotic withdrawal

### Skills

. Subinterns should be able to:

- a) Conduct a history and physical:
  - i) Recognize the clinical signs and symptoms of alcohol stimulant (cocaine, amphetamine) and opioid withdrawal

ii) Use of the Clinical Institute Withdrawal Assessment (CIWA) instrument to classify patients into stages of alcohol withdrawal

b) Develop a management plan:

- i) Treat alcohol withdrawal seizures, uncomplicated withdrawal, and Delirium Tremens (using benzodiazepines, beta or alpha blockers, anti-convulsants and/or vitamins and minerals)
- ii) Treat stimulant withdrawal using appropriate pharmacologic and non-pharmacologic methods

## Attitudes and professional behavior

Subinterns should demonstrate:

- a) A compassionate and non-judgmental attitude towards patients with active substance abuse

### Case 1

You are asked to admit a 41-year-old female presenting to the hospital from an out patient clinic for treatment of nonhealing lower extremity ulcers. On your arrival, she appears somewhat anxious but is cooperative with interview and examination. She has a 5 year history of poorly controlled type 2 diabetes mellitus and has been treated for the leg ulcers at another facility for three months with topical dressings and whirlpool therapy. She admits she is changing physicians because her previous doctor refused to give her “stronger medicine” for pain in her legs. She has been started on appropriate therapy for her leg ulcers and diabetes. You are concerned about possible substance abuse.

#### **Question 1**

***What further information do you need to obtain in evaluating possible substance abuse in this patient?***

#### **Answer:**

- details of the use of prescribed pain medications provided by her previous physician, including dosage, frequency and last dose taken
- Use of illegally obtained prescription pain medications
- Use of illicit drugs such as heroin, cocaine, frequency of use, duration of use and timing of last dose
- Smoking history
- Use of alcohol: Frequency of use, duration of use, previous problems when intake was interrupted and time of last alcoholic drink.
- Questionnaires that may be useful include CAGE, TWEAK, and AUDIT. (see appendix 1). Alcohol is the most common abused drug in the world and it has been estimated that 15%-20% of hospitalized patients may

have some degree of alcohol abuse and may experience withdrawal symptoms.

- Contacting her pharmacy might also yield more information on the pattern of her drug use

*Case continued....*

She reports daily consumption of a liter of wine for the last four years. Her last drink was approximately 8 hours ago. She has not experienced any symptoms related to lack of alcohol intake as she has not had any periods of abstinence. She was enrolled in a methadone maintenance program ten years ago but left after six months and “quit on my own”. She last used heroin two years ago. She has been taking the prescribed hydrocodone/acetaminophen 10mg/500mg (Lortab) two tablets four times daily with inadequate pain relief. She is requesting a “pain shot” especially before dressing changes. She denies any cocaine or marijuana use in the last six months. She smokes 1-2 packs of cigarettes daily.

On physical examination:

She is ill-kept and appears somewhat older than her stated age. She seems restless and easily distracted during the interview. Mild diaphoresis noted.

Vital signs: BP 150/90 mmHg Pulse 110/min, RR 18/min, Temperature 99 degree Fahrenheit

Oral mucosa is moist. Poor dental repair with multiple caries but no obvious oral abscess.

Normal heart, lung, and abdominal exam except for tachycardia

Lower extremities reveal multiple stage 3 ulcers with foul smelling greenish discharge, tender to palpation even with light touch.

Neuro exam: Patient refuses to allow testing of her reflexes due to pain. There is no tremor or focal motor deficit.

### **Question 2**

***What testing would you request along with routine admission labs and why?***

***Answer:***

***Initial Laboratory testing:***

A blood alcohol level, complete blood count, liver function tests, serum electrolytes as well as a urine toxicology screen to evaluate possible other recent substance ingestion. Overuse of the hydrocodone/acetaminophen may result in acetaminophen overdose and possible liver damage.

### **Question 3**

- a) What are some of the manifestations of alcohol withdrawal?***
- b) What are the signs and symptoms of opiate withdrawal? How does the nature of opiate affect the onset of withdrawal symptoms?***

**Answer:**

***Manifestations of Alcohol Withdrawal:***

- The time course for withdrawal from alcohol can be variable but can begin within a few hours of last alcohol consumption. Symptoms generally peak at 48-72 hours and resolve in 5-7 days.
- Risk factors for the development of severe alcohol withdrawal symptoms include:
  - history of sustained alcohol consumption,
  - age over 30 years,
  - previous symptomatic withdrawal
  - presence of other significant co-morbid illness.
- The symptoms of alcohol withdrawal can range from minor withdrawal symptoms that include tremulousness, mild anxiety, headache, diaphoresis, palpitations and nausea to frank seizures and delirium. Minor withdrawal symptoms can begin to occur 6-12 hours after last alcohol intake.
- Alcoholic hallucinosis can include visual, auditory and/or tactile hallucinations and usually appear 12-24 hours after alcohol cessation. Despite the hallucinations, the patient generally remains conversant and able to respond to questions.
- Alcohol withdrawal seizures typically occur 6-48 hours after alcohol cessation and are usually seen in patients with a long history of chronic abuse. The seizures are tonic-clonic, generalized seizures and may occur in clusters of two to six episodes.
- Alcohol withdrawal delirium also known as delirium tremens (DTs) is seen in less than 5% of hospitalized patients with symptomatic alcohol withdrawal but is the most serious and carries a mortality of up to 15%. Early recognition and aggressive treatment can reduce mortality to  $\leq 5\%$ . Symptoms include confusion, agitation, fluctuating level of consciousness, tremors, hallucinations, and evidence of sympathetic hyperactivity: dilated pupils, fevers, tachycardia, hypertension, hyperventilation and sleep disturbance

***Signs and Symptoms of opiate withdrawal:***

- Symptoms of opiate withdrawal have been compared to an influenza infection with myalgias, cough and low grade fevers.
- Other symptoms include sweating, itching, excess lacrimation, yawning, sneezing, muscle twitching and piloerection ("goose flesh") along with an intense craving for the narcotics.
- Timing of the onset of symptoms is dependent on the duration of action of the narcotic used by the patient. Drugs with short half lives, like hydrocodone and heroin result in withdrawal symptoms within 8-16 hours from the last drug dose with a peak of intensity at 36-72 hours. Longer acting opiates, like methadone and slow release morphine compounds,

may result in onset of withdrawal symptoms after 1-3 days and peak at 7-10 days.

**Question 4**

***How would you monitor this patient for possible signs/symptoms of alcohol and/or opiate withdrawal?***

**Answer:**

- The Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) [see appendix 2] is a 10 item assessment tool that can be used to monitor patients at risk for withdrawal to quantify the severity of symptoms and to monitor response to medication given to treat symptoms. Maximum possible score is 67. Scores of < 10 points correspond to minor withdrawal and include tremulousness, mild anxiety, headache, diaphoresis, palpitations and nausea. These symptoms generally begin to occur 6-12 hours after last alcohol intake. Patients with CIWA-Ar scores > 20 are at increased risk of DT's which usually occur 48-72 hours after alcohol cessation.

*Case continued...*

You prescribe hydromorphone (Dilaudid) 1 mg sq every four hours for pain with fair pain relief. At 16 hours from her last alcohol intake, she is reassessed to have a CIWA-Ar score of 26. You decide to begin treatment.

**Question 5**

- What are your treatment options?***
- What other considerations should you have when you approach the management of this patient's alcohol withdrawal symptoms?***

**Answer:**

The drugs of choice for symptomatic alcohol withdrawal are benzodiazepines.

There are two ways to approach treatment with benzodiazepines:

- *Symptom triggered dosing* has been shown to decrease hospital length of stay in patients admitted to alcohol detoxification units and generally results in significantly less medication being given. Whether that data is applicable to patients admitted to a medical/surgical service is somewhat controversial. Staff must be adequately trained to monitor symptoms with a reproducible scale, such as the CIWA-Ar and to respond appropriately to any change in patient status.
- *Fixed schedule dosing* can result in over or under medication and must be monitored by the physician with appropriate changes in dosing as indicated. Some authors endorse the use of longer acting benzodiazepines such as diazepam to avoid fluctuating drug levels which have been reported to increase likelihood of withdrawal seizures. Patients with significant liver impairment or other chronic organ dysfunction may

- have prolonged duration of action with diazepam or chlordiazepoxide. In these patients, it may be preferable to use drugs with a shorter duration of action like lorazepam or oxazepam. Oral therapy is preferable when appropriate but patients with withdrawal seizures or delirium will require parenteral therapy.
- Options for initial therapy for symptomatic alcohol withdrawal include:
    - **Chlordiazepoxide** 50-100 mg PO/IM/IV every 4-6 hr
    - **Diazepam** 5-10 mg PO every 4-6 hours
    - **Lorazepam** 1-2 mg PO/IV every 3-8 hours
    - **Oxazepam** 30-60 mg PO every 3-8 hours
  - Options for alcohol withdrawal seizures and alcohol withdrawal delirium:
    - **Lorazepam** 2-10 mg IV hourly continuous infusion (some patients will require higher dosing to control symptoms)
    - **Diazepam** 10 mg IV initially followed by 5 mg every 5 minutes until patient calm but awake
    - Once adequate symptom control is achieved, doses are decreased as tolerated over 48-96 hours.
  - Other options for pharmacologic therapy of alcohol withdrawal include:
    - **Haloperidol (Haldol)**: Has been used to control agitation but in general should be avoided as may lower seizure threshold and interfere with heat dissipation
    - **Beta-blockers** (atenolol, propranolol): Can reduce autonomic manifestations of alcohol withdrawal but do not prevent seizures and should be used only in conjunction with benzodiazepines
    - **Clonidine**: Has been used to control hypertension in acute alcohol withdrawal but does not control seizures and should be used only in conjunction with benzodiazepines
    - **Anti-seizure medications**:(barbituates, carbamazepine, valproic acid, phenytoin): May be used short term to control seizures but should not be used as monotherapy and have no role in long term use in prevention of alcohol related seizures
    - **Ethanol**: There are no controlled trials evaluating the efficacy or safety of this “old-fashioned” remedy and it should not be used for prevention or treatment of alcohol withdrawal in the hospitalized patient
  - All patients with a significant history of alcohol use should be treated with:
    - Thiamine before beginning a diet or iv solutions containing dextrose, to avoid precipitating Wernicke’s encephalopathy.
    - Electrolytes such as magnesium, potassium and phosphate levels should be monitored and replaced as indicated
    - Provided an adequately- lighted, quiet environment.
    - Physical restraints may be required for patient safety until adequate sedation is achieved with medications. Occasionally, the amount of sedation needed for control of symptoms will result in respiratory

depression, necessitating intubation and mechanical ventilation. These patients must be monitored in an ICU setting.

### Question 6

**How will you manage her presumed opiate addiction?**

**Answer:**

- *The use of opiates for pain control is appropriate in this patient.*
- *Indications for long term use of prescribed opiates is less clear especially when there is a history of polysubstance abuse and concerns for diversion of medications to finance illegal drug use.*
  - Options would include tapering opiate dosing while hospitalized or beginning long acting opiates (**methadone**) or opioid agonist-antagonist (**buprenorphine**) with intention of referral to an outpatient maintenance program.
  - **Clonidine** can lessen the symptoms of opioid withdrawal at doses of 0.1 – 0.2 mg orally every four hours and tapered after day 3. Rapid and “ultra-rapid” detoxification using protocols combining clonidine and opioid antagonists, sedatives or general anesthesia are controversial and should be carried out by experienced clinicians. There are no studies to document significant long term opiate abstinence after these rapid detoxification techniques are used.
  - Patients with alcohol and/or opiate addiction may have other substance use issues, including tobacco products, cocaine, amphetamines, and depressants. Symptoms of withdrawal may overlap and treatment of symptoms for one may mask symptoms from others. (Example: clonidine used for opiate withdrawal may blunt the autonomic responses to alcohol withdrawal, but not prevent seizures or delirium)

### Question 7:

**How will you manage this patient’s nicotine addiction?**

**Nicotine:**

- *Nicotine replacement therapy is recommended for hospitalized patients who do not wish to discontinue tobacco use and are unable to ambulate outside the facility to smoke as well as those who wish to quit but have significant withdrawal symptoms.*
- *Symptoms include intense cravings, anger, depression, anxiety, lack of concentration, insomnia and disturbing dreams.*
- *Timing of first cigarette of the day and total number of daily cigarettes are best predictors of nicotine addiction. Patients who smoke less than one pack daily and do not smoke within a few hours of awakening are less likely to require replacement therapy.*



- *Options in replacement therapies include: nicotine patch (Nicoderm, Nicotrol), gum (Nicorette), lozenge(Commit), spray (Nicotrol NS) or inhalation systems (Nicotrol inhaler).*

**Varenicline (Chantrix)** has been shown to be useful in decreasing cravings as an adjuvant to smoking cessation.

**Bupropion (Zyban)** has also been used to treat some of the symptoms of nicotine withdrawal including depression. It should not be used in patients with known seizure disorders.

## Case 2

**For each of the following scenarios identify the possible substance associated with clinical signs and symptoms.**

I) You are called to evaluate a patient while on call for increasing agitation. Patient is a 68 year old female with hypertension, depression and osteoporosis who was admitted to the hospital for left leg cellulitis 3 days ago. Patient was started on IV antibiotics and has been responding well to therapy. Patient was doing well, till about 4 hours prior to the call when the nurse noted that the patient was getting more agitated and seeing things. On examination: Patient is afebrile; BP 160/90mm Hg, HR 110/min, RR 20/min, patient is tremulous. Patient is awake, but not oriented to place or time. Patient reports seeing insects on the wall  
Neuro exam: reveals brisk bilateral reflexes but otherwise normal

### **Answer:**

**Sedative-hypnotic drugs (benzodiazepines, barbituates, “sleeping pills”):** Signs of withdrawal include elevated blood pressure, insomnia, tremulousness, agitation, generalized seizures, disorientation and hallucinations. Treatment protocols prefer **phenobarbital** or long acting benzodiazepine (**diazepam, chlodiazepoxide**).

II) A 20 year old male is brought to the ED by his family members who note that patient has been very withdrawn and not participating in family activities over the last couple of days. Patient does not have a past history of psychiatric illness, his family does state that they suspect he uses illicit drugs, but not sure of which one.

On exam, patient has stable vital signs and is in no acute distress. Patient is asleep but easily arousable. Occasional twitching is noted in his lower extremities. Rest of his physical exam is unremarkable. ECG shows J point elevation, but otherwise normal.

**Answer:**

**Stimulants (cocaine, amphetamines):** Abrupt withdrawal after prolonged use can cause severe depressive symptoms affecting appetite, sleep and psychomotor retardation. No agents have been shown to be reliably effective in treatment but indirect dopamine agonists (**methylphenidate, amantidine**), adrenergic antagonists (**propranolol**) and antidepressants (**desipramine, bupropion**) have been proposed.

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## APPENDIX 1

### Alcohol Screening Questionnaires

**CAGE** (2 or more “yes” answers = positive screen for abuse or dependence)

1. Have you ever felt the need to **Cut down** on your use of alcohol?
2. Has anyone **Annoyed** you by criticizing your use of alcohol?
3. Have you ever felt **Guilty** because of something you’ve done while drinking?
4. Have you ever taken a drink to steady your nerves or get over a hang-over? (**Eye-opener**)

**TWEAK** (2 or more “yes” answers = positive screen for abuse or dependence)

1. **Tolerance**: How many drinks can you hold ( $\geq 5$  = positive)
2. **Worry**: Have close friends or relatives worried or complained about your drinking?
3. **Eye-opener**: Have you ever taken a drink to steady your nerves or get over a hangover?
4. **Amnesia**: Has a close friend or relative ever told you about things you said or did when drinking that you could not remember?
5. **Kut down**: Have you ever felt the need to cut down on your use of alcohol?

**AUDIT** (Alcohol Use Disorders Identification Test score  $\geq 8$  = positive)

1. How often do you have a drink containing alcohol?  
(0) never (1) monthly or less (2) 2-4 x/month (3) 2-3 x/week  
(4)  $\geq 4$  x/week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?  
(0) 1 or 2 (1) 3 or 4 (2) 5 or 6 (3) 7 to 9 (4)  $\geq 10$
3. How often do you have  $\geq 6$  drinks on one occasion?  
(0) never (1) less than monthly (2) monthly (3) weekly (4) daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?  
(0) never (1) less than monthly (2) monthly (3) weekly (4) daily or almost daily
5. How often during the last year have you failed to do what was normally expected from you because of drinking?  
(0) never (1) less than monthly (2) monthly (3) weekly (4) daily or almost daily
  
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?  
(0) never (1) less than monthly (2) monthly (3) weekly (4) daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?  
(0) never (1) less than monthly (2) monthly (3) weekly (4) daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?  
(0) never (1) less than monthly (2) monthly (3) weekly (4) daily or almost daily
9. Have you or someone else been injured as a result of your drinking?  
(0) no (2) yes, but not in the last year (4) yes, during the last year
10. Has a relative, friend, or a physician or other health care worker been concerned about your drinking or suggested you cut down?  
(0) no (2) yes, but not in the last year (4) yes, during the last year

## Appendix 2

### Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

Patient: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute: \_\_\_\_\_ Blood pressure: \_\_\_\_\_

**NAUSEA AND VOMITING** -- Ask "Do you feel sick to your stomach? Have you vomited?" Observation.

- 0 no nausea and no vomiting
- 1 mild nausea with no vomiting
- 2
- 3
- 4 intermittent nausea with dry heaves
- 5
- 6
- 7 constant nausea, frequent dry heaves and vomiting

**TACTILE DISTURBANCES** -- Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.

- 0 none
- 1 very mild itching, pins and needles, burning or numbness
- 2 mild itching, pins and needles, burning or numbness
- 3 moderate itching, pins and needles, burning or numbness
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**TREMOR** -- Arms extended and fingers spread apart. Observation.

- 0 no tremor
- 1 not visible, but can be felt fingertip to fingertip
- 2
- 3
- 4 moderate, with patient's arms extended
- 5
- 6
- 7 severe, even with arms not extended

**AUDITORY DISTURBANCES** -- Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.

- 0 not present
- 1 very mild harshness or ability to frighten
- 2 mild harshness or ability to frighten
- 3 moderate harshness or ability to frighten
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**PAROXYSMAL SWEATS** -- Observation.

- 0 no sweat visible
- 1 barely perceptible sweating, palms moist
- 2
- 3
- 4 beads of sweat obvious on forehead
- 5
- 6
- 7 drenching sweats

**VISUAL DISTURBANCES** -- Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.

- 0 not present
- 1 very mild sensitivity
- 2 mild sensitivity
- 3 moderate sensitivity
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**ANXIETY** -- Ask "Do you feel nervous?" Observation.

- 0 no anxiety, at ease
- 1 mild anxious
- 2
- 3
- 4 moderately anxious, or guarded, so anxiety is inferred
- 5
- 6
- 7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

**HEADACHE, FULLNESS IN HEAD** -- Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.

- 0 not present
- 1 very mild
- 2 mild
- 3 moderate
- 4 moderately severe
- 5 severe
- 6 very severe
- 7 extremely severe

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**AGITATION -- Observation.**

- 0 normal activity
- 1 somewhat more than normal activity
- 2
- 3
- 4 moderately fidgety and restless
- 5
- 6
- 7 paces back and forth during most of the interview, or constantly thrashes about

**ORIENTATION AND CLOUDING OF SENSORIUM -- Ask**

- "What day is this? Where are you? Who am I?"
- 0 oriented and can do serial additions
  - 1 cannot do serial additions or is uncertain about date
  - 2 disoriented for date by no more than 2 calendar days
  - 3 disoriented for date by more than 2 calendar days
  - 4 disoriented for place/or person

Total CIWA-Ar Score \_\_\_\_\_  
Rater's Initials \_\_\_\_\_  
Maximum Possible Score 67

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*The CIWA-Ar is not copyrighted and may be reproduced freely. This assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.*

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Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; and Sellers, E.M. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *British Journal of Addiction* 84:1353-1357, 1989.