Withdrawal Management for Alcohol and other Substance Use Disorders

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Disclosures

<table>
<thead>
<tr>
<th>Company/Position</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkermes, a pharmaceutical firm</td>
<td>Honoraria for participation in training to be member of Speaker’s Bureau, and for Speaker’s Bureau presentations</td>
</tr>
<tr>
<td>AmmonLabs</td>
<td>Consultant and Marketing Advisor re: quality of drug testing panels, training of sales staff, customer relations</td>
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<td>Braeburn Pharmaceuticals, a pharmaceutical firm</td>
<td>Same as for Alkermes</td>
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<tr>
<td>Michael M. Miller, MD, Consulting, LLC</td>
<td>Forensic consultations, consultation to health systems and others</td>
</tr>
<tr>
<td>US WorldMeds, a pharmaceutical firm</td>
<td>Same as for Alkermes</td>
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</table>
Withdrawal Management – only one aspect of addressing substance use issues

Conditions/Substance-Related Disorders:
- Substance Intoxication
- Substance Withdrawal
- Substance Misuse / Unhealthy Use (including PDA)
- Addiction
- Substance-Induced Psychiatric Disorders
- Substance-Induced General Medical Conditions

Withdrawal Management – only one aspect of addressing substance use issues

Interventions
- Intoxication Management
- Overdose Management
* Withdrawal Management
- Management of Misuse / Brief Intervention to prevent progression
- Addiction Management (“Treatment” / “Rehab”)
- Management of Psychiatric Complications/Co-morbidities
“Detox”

“Detoxification” – the removal of a toxin
  • the brain has been poisoned
  • manifestations are changes in behavior and changes in physiology

“Detox” =
  * intoxication management
    ...counteract, replace, remove, support

  * withdrawal management
    ...drug substitution, graded dosage reduction

The ASAM Criteria
(2013 edition)
“Detox” is not “Addiction Treatment”

• Addiction
  • A chronic disease
  • Impaired control over substance use, preoccupation with substance use, continued substance use despite problems secondary to use
  • Interventions are to reduce/prevent/eliminate relapse and to promote remission of substance use

• Withdrawal
  • An acute physiological disturbance, time-limited

Withdrawal vs. Addiction

• WITHDRAWAL:
  an acute physiological disturbance, time-limited

• ADDICTION (DSM-5 “Substance Use Disorder”):
  a chronic, behavior disorder

• Management of Withdrawal (‘detox’)
  is not treatment of addiction!
  (but it may be needed to prepare patient to engage with treatment)
Important Withdrawal Syndromes

- Corticosteroids
- Beta blockers
- Tricyclics and SSRIs
- Opioid analgesics
- Sedative-hypnotics
- Ethanol
- Stimulants (caffeine)
  - Generally, what you do is ‘taper’ = “safe drug discontinuation”
- Nicotine
- Cannabis

Basic Principles of Detox

- Provide calm environment for the patient, to reduce anxiety that would amplify symptoms (regardless of the drug class)
- Replace the missing substance with a pharmaceutical that is cross-tolerant with the drug the patient is withdrawing from (or is an agonist at the same neurotransmitter receptor)
- **Stabilize the patient**—use whatever dose is necessary to have the patient ‘not in withdrawal, not intoxicated’, but stable*
- Institute a **step-wise graded reduction** in the replacement substance*

* ... attributions to David E. Smith, MD, HAFCI, San Francisco, CA
An Overview of Withdrawal Management

- Alcohol / Sedative Withdrawal is potentially life-threatening – *this is the biggie*
- **Opioid Withdrawal is uncomfortable, but not dangerous**
- **Persons with Opioid Addiction are exquisitely sensitive to subjective discomforts / don’t tolerate them**
- Cocaine Withdrawal is insignificant physiologically-- but can be significant psychiatrically (suicide)
- Nicotine Withdrawal is common and treatable
- Cannabis Withdrawal is a real thing
- Caffeine Withdrawal is easy: fixed schedule of reduction

Two Components to Opioid Withdrawal

- *Autonomic Withdrawal*: tolerance in the NE-ergic locus coeruleus to opioids (4+), EtOH/sedatives (3+), and others (1+), leading to high BP, HR, diaphoresis, peristalsis, irritability when agent is withdrawn (rx is with clonidine/guanfacine/lofexidine, β blockade)
- **Affective Withdrawal**: tolerance in the DA-ergic mesolimbic reward system to cocaine (4+), stimulants (3+), and opioids (2+), cannabinoids (2+) and EtOH/sedatives (2+); nucleus accumbens is #1 site; withdrawal of agent leads to dysphoria and return to use (rx is to replace with original agent or cross-tolerant agent, or with bupropion to offer ↑ dopamine tone)
**Sedative Withdrawal**

**Symptoms & Signs**

- Anxiety / agitation
- Tremor
- Nausea
- Hypertension
- Tachycardia
- Hyperreflexia
- Diaphoresis
- Looks to some like hypomania
- Hypersensitivity to stimuli
- Hallucinosis
- Deper
- sonalization
- Psychosis
- Seizures
- Delirium

*See why people use the term alcohol/sedative withdrawal syndrome?*

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**Stages of Alcohol Withdrawal Syndrome (AWS)**

- **Stage 1**
  - Autonomic signs/symptoms
    - \( \uparrow \) HR, \( \uparrow \) SBP, orthostatic hypotension, sweats, mydriasis, nausea, \( \uparrow \) temp
  - Behavioral signs/symptoms
    - Irritability, agitation, insomnia
  - Tremor, hyperreflexia

- **Stage 2**
  - hallucinosis

- **State 4**
  - seizures
    - Generalized, with post-ictal confusion
    - Tongue-biting; but no incontinence
    - Peak risk 6-72 hrs

- **Stage 4**
  - delirium
    - “Delirium tremens” – more likely if previous episodes, stress caused by medical illness/surgical illness/injury
Shakes

➢ Assess for tremor of skeletal muscles (observe for hand tremor, tongue tremor, eyelid tremor)
➢ Remember that patients may try to consciously suppress or amplify this symptom
➢ Other things can cause a tremor, or look like the tremor of alcohol withdrawal: anxiety, caffeine, lithium, asthma inhalers, ‘benign familial tremor’

Sweats

➢ Sweats (look for beads of sweat, at hair line of forehead and on back of the neck)
➢ They’ll rationalize: oh, it’s just a warm room, or heavy covers on the bed
➢ Or maybe it’s not a rationalization—menopause, other health care condition
Stage Two - AWS

- Worsening symptoms and signs of Stage I
- Defined by presence of hallucinosis
  - Auditory > Visual > Tactile
- Typically starts 24 to 72 hours after last drink
- Occurs in 2-8% of untreated individuals (JAMA 2018, references 16 and 17)
- Patient still cognitively intact

Stage Three - AWS

- Withdrawal Seizures - 5 to 15% of untreated individuals
- Typically within the first 48 hours after the last drink
- Always Grand Mal - short duration of tonic/clonic seizure
- Occur in Salvoes
- 3% will enter Status Epilepticus
**Stage Four - AWS**

- Delirium Tremens (DTs)
- Begins 48 hours to 14 days after last drink
- Profound clouding of the sensorium – i.e., patient is delirious, and often has significant paranoid delusions
- Mortality = approximately 5%
- Approx. 5% of untreated individuals will enter Stage 4
- Approx. 1/3 or patients with Stage 3, if untreated, will progress to Stage 4 (JAMA 2018, reference 20).

**Alcohol Withdrawal Delirium**

Delirium = Delirium = Delirium
- Acute Brain Failure
- Clouded sensorium = disoriented and incoherent (no logical structure to language)
- Misidentification of others
- Hallucinations
  - Without insight that they are not real
  - Often frightening → can result in staff being threatened
- Agitation → marked ↑ activity / absence of sleep
Alcohol Withdrawal Delirium

- Late phase phenomenon cf. Stages 1-3 which are early phase
- Delirium due to alcohol withdrawal lasts several hours – days
- Delirium from sedative (benzo) withdrawal can last several days-weeks
- Be sure to consider other causes of delirium – it could be due to another cause, or it could be multifactorial (“ticks and fleas”)

Alcohol Withdrawal Delirium and Mortality

- Autonomic storm
- Hyperthermia can be cause of death
- Also, can lose so much fluid from sweating and panting that electrolyte disturbance can cause arrhythmia
- Specifically, there is hypo Mg and hypo P in DT’s
- More often, mortality is due to cardiovascular collapse: heart rate is so fast that ventricles cannot refill → cardiac output drops
Is it really what they say it is?

• They can say they’ve had a seizure—but maybe they just got weak in the knees and fell to the ground, or had myoclonic jerks
• They can say they’ve had D.T.’s—but maybe they just had severe Stage I (really dramatic shakes and agitation) and/or Stage II symptoms (most patients and many doctors and nurses think that any hallucinations mean that the person is in Delirium Tremens and many patients and lay observers will say a patient in very severe Stage I has had “D.T.’s”)

Prognosticators of Severe Withdrawal

• BAC greater than 300mg/dl
• Age greater than 35 years
• Previous AWS seizure
• Concomitant medical or surgical problem
• Abnormal liver functions
• Other drug use - especially sedatives/hypnotics
Prognosticators of Severe Withdrawal

- BAC greater than 300mg/dl
- Age greater than 35 years
- **Previous AWS seizure**
- Concomitant medical or surgical problem
- Abnormal liver functions
- Other drug use - especially sedatives/hypnotics


- The single best predictor of developing DT’s is: h/o previous episode of DT’s
- The best predictor overall of SAWS is the PAWSS Score (Prediction of Alcohol Withdrawal Severity Scale); see Maldonado JR, et al., *Alcohol and Alcoholism (U.K.)*, 50:509-18, 2015.
**Kindling Phenomenon**

- Each subsequent withdrawal episode is worse
- Medical management of AWS may prevent the kindling phenomenon
- Evidence better with anticonvulsants such as valproic acid & carbamazepine than benzodiazepines & barbiturates in blocking progression of the kindling phenomenon.

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**Alcohol Withdrawal Management**

1. Replace Sedative (T.A.U., except in VA et al.)
2. Prevent Advancing to Higher Stages
   - I II III IV
3. Treat hallucinosis
4. Consider other causes of seizures, especially if > 48 hours after falling BAC
5. Manage the delirium
6. Identify and manage co-morbid medical conditions
Pathophysiology/mechanism of AWS

• It’s not just about norepinephrine and dopamine
• It’s about the balance of effects via GABAergic and glutamatergic pathways
• Recall the basic neurochemistry of glutamate and GABA.

Treatment of A.W.S.


• Wartenberg AA. ASAM Principles of Addiction Medicine, 5th Ed., 2014
Strategies of Sedative Replacement

• Fixed dose protocols, with pre-designed taper
• Loading with long-acting benzo
• Symptom-triggered (all based on signs/symptoms)
  • CIWA-A-r scale for quantification of “severity of illness”

Strategies of Sedative Replacement

• Fixed dose protocols, with pre-designed taper
  • Librium 100 QID x 1 d, 75 QID x 1 d, 50 QID x 1 d, 25 QID x 1 d; or 100 QID then TID then BID then QD

• Loading with long-acting benzo
  • “How many drinks can you drink without showing effects?”
  • Load with the dose to which patient is tolerant
    ➢ One standard drink = 5 mg diazepam
“Standard Drink’ =

- 0.6 oz of 100% ethanol = 13 gm.
- 12 oz of 5% beer
- 5 oz of 12% wine
- 1.5 oz of 80-proof liquor
Symptom-triggered based on CIWA Scale

- Maximum score possible 67
- < 8 = mild
- 8 - 15 = moderate
- > 15 = severe

Some say treat with benzo’s for moderate, and refer to general medical facility for severe

Miller protocol

- 6 or greater = 5 mg diazepam
- 12 or greater = 10 mg diazepam
- 18 or greater = 15 mg diazepam
- 24 or greater = 20 mg diazepam

https://slideplayer.com/slide/10322009/
### CIWA-Ar scale

**Nausea/vomiting:** “Do you feel sick to your stomach? Have you vomited?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No nausea or vomiting</td>
</tr>
<tr>
<td>1</td>
<td>Intermittent nausea with dry heaves</td>
</tr>
<tr>
<td>2</td>
<td>Nausea, constant, frequent dry heaves and vomiting</td>
</tr>
</tbody>
</table>

**Tremor:** Arms extended and fingers spread apart

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No tremor</td>
</tr>
<tr>
<td>1</td>
<td>Tremor not visible but can be felt fingertip to fingertip</td>
</tr>
<tr>
<td>2</td>
<td>Moderate with patient's arms extended</td>
</tr>
<tr>
<td>3</td>
<td>Severe, even with arms not extended</td>
</tr>
</tbody>
</table>

**Paroxysmal sweats**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No sweat visible</td>
</tr>
<tr>
<td>1</td>
<td>Barely perceptible sweating, palms moist</td>
</tr>
<tr>
<td>2</td>
<td>Beads of sweat obvious on forehead</td>
</tr>
<tr>
<td>3</td>
<td>Drenching sweats</td>
</tr>
</tbody>
</table>

**Anxiety:** “Do you feel nervous?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No anxiety, at ease</td>
</tr>
<tr>
<td>1</td>
<td>Mildly anxious</td>
</tr>
<tr>
<td>2</td>
<td>Moderately anxious, or guarded, so anxiety is inferred</td>
</tr>
<tr>
<td>3</td>
<td>Equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions</td>
</tr>
</tbody>
</table>

**Headache, fullness in head:** “Does your head feel different? Does it feel like there is a band around your head?” Do not rate for dizziness or light-headedness. Otherwise, rate severity.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Very mild</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe</td>
</tr>
</tbody>
</table>

### Agitation

**META PHI 2015**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Normal activity</td>
</tr>
<tr>
<td>3</td>
<td>Somewhat more than normal activity</td>
</tr>
<tr>
<td>4</td>
<td>Moderately fidgety and restless</td>
</tr>
<tr>
<td>5</td>
<td>Paces back and forth during most of the interview, or constantly thrashes about</td>
</tr>
</tbody>
</table>

**Tactile disturbances:** “Have you had any itching, pins and needles sensations, any burning or numbness, or do you feel bugs crawling on your skin?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Very mild itching, pins and needles, burning, or numbness</td>
</tr>
<tr>
<td>2</td>
<td>Mild itching, pins and needles, burning, or numbness</td>
</tr>
<tr>
<td>3</td>
<td>Moderate itching, pins and needles, burning, or numbness</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe hallucinations</td>
</tr>
<tr>
<td>5</td>
<td>Severe hallucinations</td>
</tr>
<tr>
<td>6</td>
<td>Extremely severe hallucinations</td>
</tr>
<tr>
<td>7</td>
<td>Continuous hallucinations</td>
</tr>
</tbody>
</table>

**Auditory disturbances:** “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?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Very mild harshness or ability to frighten</td>
</tr>
<tr>
<td>2</td>
<td>Mild harshness or ability to frighten</td>
</tr>
<tr>
<td>3</td>
<td>Moderate harshness or ability to frighten</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe hallucinations</td>
</tr>
<tr>
<td>5</td>
<td>Severe hallucinations</td>
</tr>
<tr>
<td>6</td>
<td>Extremely severe hallucinations</td>
</tr>
<tr>
<td>7</td>
<td>Continuous hallucinations</td>
</tr>
</tbody>
</table>

**Visual disturbances:** “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?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Very mild sensitivity</td>
</tr>
<tr>
<td>2</td>
<td>Mild sensitivity</td>
</tr>
<tr>
<td>3</td>
<td>Moderate sensitivity</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe sensitivity</td>
</tr>
<tr>
<td>5</td>
<td>Severe hallucinations</td>
</tr>
<tr>
<td>6</td>
<td>Extremely severe hallucinations</td>
</tr>
<tr>
<td>7</td>
<td>Continuous hallucinations</td>
</tr>
</tbody>
</table>

**Orientation and clouding of sensorium:** “What day is this? Where are you? Who am I?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Oriented and can do serial additions</td>
</tr>
<tr>
<td>1</td>
<td>Cannot do serial additions or is uncertain about date</td>
</tr>
<tr>
<td>2</td>
<td>Disoriented for date by no more than 2 calendar days</td>
</tr>
<tr>
<td>3</td>
<td>Disoriented for place by more than 2 calendar days</td>
</tr>
<tr>
<td>4</td>
<td>Disoriented for place and/or person</td>
</tr>
</tbody>
</table>

- **Score of 10+** indicates need for benzodiazepines
- **Discontinue treatment when score < 8 on two consecutive occasions**
SHOT Scale

| Sweating          | 0 – No visible sweating  
|                   | 1 – Palms moderately moist  
|                   | 2 – Visible beads of sweat on forehead   
| Hallucinations    | 0 – No hallucinations  
|                   | 1 – Tactile hallucinations only  
|                   | 2 – Visual and/or auditory hallucinations   
| Orientation       | 0 – Oriented  
|                   | 1 – Disoriented to date by one month or more  
|                   | 2 – Disoriented to place or person   
| Tremor            | 0 – No tremor  
|                   | 1 – Minimally visible tremor  
|                   | 2 – Mild tremor  
|                   | 3 – Moderate tremor  
|                   | 4 – Severe tremor   

• Score of 2+ indicates need for benzodiazepines  
• Discontinue treatment when score < 2 on two consecutive occasions

Protocol: Symptom-Triggered Treatment of Alcohol Withdrawal (1)

1. Diazepam treatment  
   • 10-20 mg PO q 1-2 H when CIWA ≥10 or SHOT ≥2  
   • If cannot take diazepam orally, use lorazepam, or give IV diazepam at a rate of no more than 2-5 mg/min
Diazepam: Precautions

- Can cause sedation if:
  - Patient intoxicated (estimated BAL > 30-40 mmol/l)
  - Liver dysfunction
  - Elderly patients
  - Low serum albumin
  - On methadone or high doses of opioids
- Can trigger encephalopathy in patients with decompensated cirrhosis
- Can cause respiratory depression in patients with severe COPD, asthma or pneumonia

Symptom-Triggered Treatment of Alcohol Withdrawal (2)

2. Lorazepam
   - 2-4 mg PO, SL, IM, IV q 1-2 H
   - Shorter duration of action than diazepam
   - Safer in patients at high risk for diazepam toxicity:
     - Liver dysfunction, elderly, low serum albumin, on methadone or high dose opioids, decompensated cirrhosis, respiratory impairment
Diazepam Vs. Lorazepam

<table>
<thead>
<tr>
<th></th>
<th>Diazepam</th>
<th>Lorazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing Equivalents</td>
<td>5 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Dispensing for</td>
<td>10-20 mg PO q 1-2 H</td>
<td>2-4 mg PO, SL, IM, IV q 1-2 H</td>
</tr>
<tr>
<td>withdrawal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of action</td>
<td>Up to 5 days</td>
<td>12 hours</td>
</tr>
</tbody>
</table>

SSA uses vital signs in the scale

- Selective Severity Assessment
- Actually, the MSSA.
Alcohol Detox
(Sedative Replacement)

- Benzodiazepines
- Other sedatives will work but have disadvantages—barbiturates, ethanol, paraldehyde
- [ Other sedating drugs that aren’t cross-tolerant with EtOH won’t work, e.g. phenothiazines ]

There are different ways to skin a cat

- Sedative replacement (benzos much preferred to barbiturates; long-acting oral benzos preferable to short-acting, unless a good reason to use a short-acting – e.g., lorazepam)
- Anticonvulsants
  - Carbamazepine
  - Valproate
  - Gabapentin
Non-benzo Withdrawal Management Methods

- Carbamazepine
  - 100mg every 6 hours
  - 100mg every 8 hours if weight less than 100 pounds
  - 200mg every 8 hours if weight more than 220 pounds
  - Baseline CBC and hepatic panel

- Divalproex
  - 250mg every 6 hours
  - 250mg every 8 hours if weight less than 100 pounds
  - 500mg every 8 hours if weight more than 220 pounds

- Gabapentin 300 mg/dose using CIWA (symptom-triggered)

Advantages of Anti-Convulsant Approach

- Less oversedation
- Less ataxia/falls
Disadvantages of Anti-Convulsant Approach

• Do they only treat Stages 1-2?
• Do they protect against delirium, especially in a patient with a history of DT’s?
• They aren’t effective for preventing Alcohol Withdrawal Seizures
  • By the time the serum level is ‘therapeutic’ for anti-seizure effect, the time of maximum risk for alcohol withdrawal seizures has passed!
• The best protection vs. Stage 3 withdrawal, especially in a patient with a history of alcohol withdrawal seizures, is a benzo, esp. I.V.

Sedative Withdrawal (from benzos, Z-drugs, barbs (Fiorinal®), GHB/1,4 GBL, propofal)

• Similar to alcohol withdrawal--though usually not as dramatic or obvious and more variability; often VS are normal and CIWA is low

• Dependent on
  ✓ Duration of sedative use
  ✓ Daily amount of sedative use
  ✓ Half-life of sedative used
Sedative Withdrawal

- Declining serum levels correlate with emergence of withdrawal symptoms
  - Shorter acting Bzdz withdrawal begins within 24 hours of cessation & peaks within 1 to 5 days
  - Longer acting Bzdz withdrawal begins within 5 days of cessation & peaks within 1 to 9 days
- Duration of withdrawal
  - 7 to 21 days for shorter acting Bzdz
  - 10 to 28 days for longer acting Bzdz

Benzodiazepine Duration of Action

- Short-Acting (half life < 3 hours)
  - Triazolam
- Intermediate-Acting (half life 12-20 hours)
  - Oxazepam Temazepam Lorazepam
  - Alprazolam Estazolam
- Long-Acting (half life > 100 hours)
  - Diazepam Chlordiazepoxide Chlorazepate
  - Clonazepam Flurazepam
Sedative Withdrawal Management

- Replace and taper
- Substitute and taper
- Symptom-triggered (not recommended)
- Anticonvulsant method

Tapering

- Can stabilize patient (first step always) on *their* drug, but...
- Usually SUBSTITUTE with a long-acting sedative and taper that, not the original agent
- Give the patient a calendar with a tapering schedule
- Write prescriptions that will be filled every day or every other day
- Write the date that the Rx is to be filled
- Use one pharmacy only – discuss plan with the pharmacist
Substitution Agents

- Usually phenobarbital or clonazepam
- Use clonazepam for alprazolam
- Phenobarbital best to use when
  - High dose of sedatives
  - Unknown agents or mix of agents, or erratic use
- Phenobarbital intoxication not well liked
- Once steady state achieved, negligible inter-dose serum level variation

Tapering with or without Substitution

- Phenobarbital – on initial dose for two days
  - If no signs of withdrawal or intoxication begin taper on day 3
    - Taper over about a 20 day period
    - Reduce dose by 30-60mg per day
    - Final 25% make smaller daily dose reductions
- Benzodiazepine tapering
  - Provide daily amount in divided doses
  - About 25% reduction per week of starting dose or about 1mg clonazepam per week – which ever is less
  - Final 25% of reduction can/should be slower: 10% every week
### Substitution Dose Conversions

- **Phenobarbital 30mg**
- **Diazepam 10mg**
- Chlordiazepoxide 25mg
- Clonazepam 2mg
- Flurazepam 15mg
- Lorazepam 2mg
- Oxazepam 10mg
- Temazepam 15mg
- **Triazolam 0.25mg**
- Butalbital 100mg
- Meprobamate 400mg
- Carisoprodol 700mg
- Chlortal Hydrate 500mg
- **Two standard drinks**

### ‘Standard Drink’ =

- 0.6 oz of 100% ethanol = 13 gm.
- 12 oz of 5% beer
- 5 oz of 12% wine
- 1.5 oz of 80-proof liquor
**Writing Prescriptions for Future Pick-Up**

- Write amount to be dispensed out in English and draw a box around this
- Write zero refills
- Date prescription today’s date 10/21/04 but then write fill only on 10/23/04
- Number prescriptions in chronological order
- Make photocopies of your prescriptions for your files
- If patients make accusations regarding the pharmacist, refer them to the state pharmacy board

---

**Non-benzo Withdrawal Management**

- **Carbamazepine**
  - 100mg every 6 hours
    - 100mg every 8 hours if weight less than 100 pounds
    - 200mg every 8 hours if weight more than 220 pounds
  - Baseline CBC and hepatic panel
- **Divalproex**
  - 250mg every 6 hours
    - 250mg every 8 hours if weight less than 100 pounds
    - 500mg every 8 hours if weight more than 220 pounds
- On fourth day, check pre-dose serum level (5 half lives)
Sedative Detox—Overview of Three Approaches

• Replace with their own sedative, and taper (21-120 days)
• Replace with long(er)-acting sedative (phenobarbital, clonazepam) that hasn’t been self-reinforcing for them, then taper (21-30 days)
• Use atypical anticonvulsants (carbamazepine, valproate), then do rapid taper of the sedative-hypnotic once a therapeutic serum level has been attained/confirmed (taper over 4-7 days)
• Anticonvulsant can be kept in place for 30 days then taper it away over 2-4 weeks (unless gabapentin was agent used and you want to keep that in place to treat addiction involving alcohol use: see Annals of Internal Medicine, Barbara Mason et al., January 2014).

Wrapping up the Anticonvulsant Approach

• Once therapeutic on anti-convulsant, begin taper of sedative dose
  • 75% pretreatment dose on day one
  • 50% pretreatment dose on day two
  • 25% pretreatment dose on day three
  • On day four give no further sedatives

• Continue anticonvulsant between 30 to 60 days then taper over 4 to 8 days
  • Recheck hepatic panel and CBC at 1 to 3 week intervals for Carbamazepine
**Sedative Tolerance Test**

- Pentobarbital 200mg initially then 100mg every one hour
  - Assess for signs of intoxication
  - Convert to phenobarbital at a conversion of pentobarbital 100mg = Phenobarbital 30mg
- Pentobarbital is out of production; can use any long-acting sedative
- Need to design a different sedative taper test

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**Opioid Use Disorder: Withdrawal Management and Addiction Treatment**

Michael M. Miller, MD, DFASAM, DLFAPA

A Comprehensive Review of Pain Medicine  
Office of Continuing Professional Development (OCPD)  
UW School of Medicine and Public Health  
Fluno Center, UW Madison  
August 16, 2018
Opioid Withdrawal Management

- The Harrison Act of 1914 made it illegal for a physician to prescribe and opioid to a patient for the treatment of opioid addiction or withdrawal
- So a physician cannot ‘detox’ a patient using the opioid the patient is taking (OxyContin, Demerol, Darvon) or using any other opioid....

Opioid ‘Detoxification’

- But a physician can, legally, outline a plan for discontinuation of a therapy that he/she started
- Opioid DISCONTINUATION in cases of chronic pain patients who need their dose decreased due to tolerance, opioid-induced hyperalgesia, lack of efficacy, adverse effects, or ‘misuse’, is LEGAL
- You write the Rx, and put on the Rx and in your progress note “therapeutic taper”; you do not use the term “detox”
Opioid Withdrawal Management ("Detox")—Agents which can be legally used

- Methadone (only in an OTP)
- Buprenorphine (by any physician with a DEA waiver)
- Clonidine (also: guanfacine, lofexidine)
- But with Alpha2 agonists, add supplemental agents for symptom relief
  - for anxiety, insomnia, aches, nausea, diarrhea, cramping, dehydration

- Any opioid will work – but all others are **illegal**!
- What this slide *doesn’t* say!
  - *it may make common sense, but it is NOT legal to use any other opioid (e.g., the one the patient is on) to do “detox” if the patient has addiction*

Literature Review

Opioid Withdrawal

- Insomnia
- Irritability / Restlessness
- Anxiety / Dysphoria / Lability
- Nausea / Anorexia
- Abdominal cramps / Diarrhea
- Arthralgias / Myalgies
- Jitters / Runny Nose / Runny Eyes / Yawn / Sneeze
- Flu-like malaise and whole-body aches
- Pupillary dilatation

Evaluation: Opioid Withdrawal

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yawning</td>
<td>Mydriasis</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Sweating</td>
<td>Piloerection</td>
<td>Increased Pulse</td>
</tr>
<tr>
<td>Lacrimation</td>
<td>Muscle Twitching</td>
<td>Increased Resp Rate</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>Anorexia</td>
<td>Elevated BP</td>
</tr>
</tbody>
</table>

* Source: Adapted from TIP #24. A Guide to Substance Abuse Services for Primary Care Clinicians. DHHS (SMA) 97-3139, 1997
C.O.W.S.


S.O.W.S. – Subjective Opioid Withdrawal Scale (a 10-item self-rating scale)

• Gossop M. Addictive Behaviors 15:487 (1990)

OWS Mechanism

• When an opioid (an agonist at the mu opioid receptor) engages the receptor, the “second messenger” is cAMP, and that decreases norepinephrine (NE) activity at the end of the axon, leading to
  • Diminished arousal/alterness (drowsiness)
  • Diminished awareness of pain (anti-nociception)

• With chronic opioid administration, NE-ergic systems are up-regulated to maintain homeostasis

• With significant decrease or abrupt cessation of opioid agonist activity, the upregulated NE activity, now unopposed by opioids, is manifest as increased sympathetic activity (↑HR, ↑BP, ↑tremor, irritability, agitation, shivers, gooseflesh)

Opioid Withdrawal Symptoms

• Timing of Onset, and timing of Peak symptoms, depend on opioid or opiate used – variable to the individual

• Heroin - onset 8 hours, with peak symptoms 24 to 48 hours after last use

• Methadone - onset 24-48 hours, with peak symptoms 48 to 96 hours after last use

• Subjective symptoms may persist for days
Opioid Withdrawal

- For opioids with longer half-lives (e.g., methadone), there is a longer period before onset (methadone: 36-72 hours), longer period before peak effects occur
- Medications with longer half-lives generally have less severe spontaneous withdrawal syndromes
- Medications with shorter half-lives generally are more ‘addicting’
  - **But: the intensity of subjective withdrawal symptoms is ** NOT a function of opioid dose! **

Opioid Withdrawal Management

- **The LAW is tricky**
- **Harrison Act of 1914:** it is illegal for a doctor to prescribe an opioid to an opioid addict for the management of opioid addiction or opioid withdrawal
  - **Exception #1:** methadone *in a MMT clinic*
  - **Exception #2:** buprenorphine *by a waived doc*
‘Detox’ isn’t the same as “therapeutic discontinuation”

- ANY DOC can discontinue a plan of care (chronic opioid analgesic therapy, ‘C.O.A.T.’) if you have a general DEA registration
- Thus, you can TAPER a person who is PHYSICALLY DEPENDENT but who does not have ADDICTION
- But you CANNOT TAPER an opioid (says the DEA) in a person who has addiction (e.g., using ‘street’ supplies); i.e., if you think it is addiction, you can’t legally taper Darvon with Darvon, Vicodin with Vicodin, etc.

Two Components to Opioid Withdrawal

- **Autonomic Withdrawal:** tolerance in the NE-ergic locus coeruleus to opioids (4+), EtOH/sedatives (3+), and others (1+), leading to high BP, HR, diaphoresis, peristalsis, irritability when agent is withdrawn (rx with clonidine, β-blocker)
- **Affective Withdrawal:** tolerance in the DA-ergic mesolimbic reward system to cocaine (4+), stimulants (3+), and opioids (2+), cannabinoids (2+) and EtOH/sedatives (2+); nucleus accumbens is #1 site; withdrawal of agent leads to dysphoria and return to use; (rx with agonist replacement; some use bupropion in cases other than alcohol/sedative withdrawal)
Mechanism of Action of α-adrenergic agonists

• Site of action is presynaptic receptor that serves as negative feedback loop, to inhibit NE tone
• Result is ↓BP, ↓HR, ↓agitation, resolution of insomnia and other physical manifestations
• The locus coeruleus is where NE neurons are concentrated.

Clonidine-Method Detox -- details

• Clonidine 0.1 mg every 4-6 hours (or a patch)
• Diminishes symptoms, but not 100%
• Supplemental meds needed
  ➢ ibuprofen
  ➢ Bentyl for cramps
  ➢ loperamide for diarrhea
  ➢ Tigan or Zofran for nausea
  ➢ benzo’s for daytime anxiety / insomnia @ HS
    • It’s okay to use benzo’s, short-term, for opioid detox
    • lorazepam 0.5 mg four times daily for anxiety; can also offer 1-2 tabs for insomnia; but some use zolpidem instead
    • trazodone not advised: hypotension, QT prolongation
Clonidine Protocol – clonidine dosing

- Oral 5 day supply; or prescribe a clonidine transdermal patch “0.1mg” daily for 7 days
- Generally keep patch on x 7 days, and offer 5-day supplies of supplemental agents
- Whether p.o. or patch, advise patient of potential side effects of sedation and orthostatic dizziness, and that they stop the oral, or even the patch, if symptomatic
- Best practice is to check ortho BP in your office daily (maintain close contact during detox)
- Half-doses of oral (0.05) can be used if needed
- Taper over 2 days at end of this regimen, to prevent rebound hypertension

Clonidine-Method Detox – dosing

- Clonidine diminishes symptoms, but not 100%
- Supplemental P.R.N. meds are usually needed
  - ibuprofen (400 mg four times daily)
  - Bentyl for cramps (20 mg four times daily)
  - loperamide for diarrhea (2 mg four times daily)
  - Tigan or Zofran (4 mg four times daily)
  - benzo’s for daytime anxiety / insomnia @ HS
    - It’s okay to use benzo’s, short-term, for opioid detox
    - lorazepam 0.5 mg four times daily for anxiety; can also offer 1-2 tabs for insomnia
- Generally keep patch on x 7 days, and offer 5-day supplies of supplemental agents
Can use other α 2A-adrenergic receptor agonists

- Clonidine
- Guanfacine
- Lofexidine (U.K. – and now FDA approved new agent
  - LUCEMYRA™ (lofexidine) tablets 0.18mg
  - FDA approved 5/16/2018
  - Dose is 3 tabs QID for 5-7 days (FDA says up to 14 days of Rx is OK)
  - Taper for 2 days at the end (e.g., 2 tabs QID s 1 d, 1 tab QID x 1 d)
  - Use 2 tabs QID instead of 3 if hepatic or renal impairment

An example of a real-world protocol

Medical Director, Meriter/NewStart, 1989-2010
Addiction Medicine Consultation and Evaluation Service (AMCES)
Now: UnityPoint Health/Meriter)
NewStart outpatient protocol

- **Clonidine 0.1mg** - ½ tablet PO 3-4x daily for OWS
  - *hold for 12 hours if becomes light-headed or dizzy upon standing or experiences excessive daytime fatigue*
  - (Dispense 0.1 mg #10.)**

- **Trazodone 50mg** – One tablet PO HS as needed for insomnia; may repeat 50 mg PO in 1 hour if needed.
  - (Dispense 50 mg #10.)**
  - *Warn of morning dry mouth, fatigue & dizziness upon standing; consider decreasing to ½ tablet (25 mg) if side effects noted.*

**PO medications should be filled for a 5 day supply only.**
Clonidine Protocol

• Oral 5 day supply, or clonidine transdermal patch “0.1mg” daily for 7 days
• Generally keep patch on x 7 days, and offer 5-day supplies of supplemental agents
• Whether p.o. or patch, advise patient of potential side effects of sedation and orthostatic dizziness, and that they stop the oral, or even the patch, if symptomatic
• Best practice is to check ortho BP in your office daily (maintain close contact during detox)
• Half-doses of oral (0.05) can be used if needed

Summary:
Standard Treatment for Opioid W/D
(true ‘detox’ in a case of addiction)

• Stop opioid abruptly
• Provide comfort using alpha2 agonist (non-controlled substance, anyone can prescribe)
  • clonidine, guanfacine, lofexidine
  • tizanidine could work but many contraindications (CYP1A2 inhibitors including contraceptives)
• Realize that clonidine relieves only autonomic symptoms of withdrawal
• Realize that OPIOID WITHDRAWAL WON’T HURT THE PATIENT, they’ll just complain a lot!
Buprenorphine

Partial $\mu$ agonist with high affinity
   – Will displace any other $\mu$ agonist precipitating withdrawal
A variety of formulations are FDA approved for pain management:
• Buprenex® - injectable form of buprenorphine HCl - only indication is for analgesia; 0.3 mg = 10 mg parenteral morphine sulfate; DEA forbids use for detox in a person with addiction
• BuTrans® - transdermal patch; DEA forbids use for addiction treatment
• Belbuca® - buccal film for analgesia; many dosage strengths from 75 to 900 mcg

Buprenorphine for pain

• ANY provider can prescribe bupe for pain as:
  • Butrans® patches (q 7 days)
  • Belbuca® (buccal film, q 12-24 hrs)
Buprenorphine

- Partial mu agonist with high affinity
  - Will displace any other mu agonist precipitating withdrawal
- Suboxone® – buprenorphine/naloxone combination, e.g. 2/0.5 mg or 8/2 mg; originally sublingual tablets; **now only available as ‘film’** in various strengths: 2 mg, 4 mg, 8 mg, and 12 mg of buprenorphine in 4:1 ratio with the naloxone
- Generic buprenorphine (formerly also Subutex®)
  - 2 & 8mg sublingual tablets
- Zubsolv® tablets
- Bunavail® film (buccal)

A bit of a lesson in pharmacology is helpful in understanding buprenorphine

- How it works
- How is can precipitate withdrawal if you give it to someone on a full opioid agonist
Classification of Ligands by Effect on Mu opioid receptor ("the morphine receptor")

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agonist</td>
<td>Morphine-like effect (e.g., heroin)</td>
</tr>
<tr>
<td>Partial Agonist</td>
<td>Weak morphine-like effects with strong receptor affinity (e.g., buprenorphine)</td>
</tr>
<tr>
<td>Antagonists</td>
<td>No effect in absence of an opiate or opiate dependence (e.g., naloxone, naltrexone)</td>
</tr>
</tbody>
</table>

Functions of Drugs at Receptors

**Full agonists:**
- Occupy the receptor and activate that receptor
- Increasing doses of the drug produce increasing receptor-specific effects until a maximum effect achieved
- Most abused opioids are full agonists
- Examples of full agonist opioids: heroin, methadone, morphine, oxycodone
Functions of Drugs at Receptors

**Partial agonists:**
- Bind to and activate receptor
- Increasing dose does not produce as great an effect as does increasing the dose of a full agonist (less of a maximal effect is possible)
- Buprenorphine (Suboxone®, etc.) is the newest “partial agonist”
  - Butorphanol (Stadol®)
  - Pentazocine (Talwin®)
  - Nalbuphine (Nubain®)

Functions of Drugs at Receptors

**Antagonists:**
- Bind to receptors but don’t activate the receptor
- Block the receptor from activation by full and partial agonists
Activity: Full Agonist (Morphine), Partial Agonist (Buprenorphine), Antagonist (Naloxone)
A New Formulation to Reduce Diversion

Suboxone® Film (sub-lingual)
Advanced BEMA Delivery

**BEMA: BioErodible MucoAdhesive**

*Unique 2-layer design is the basis for differentiation*

The printed *mucoadhesive layer* with active drug goes on the inside of the cheek.

The **backing layer** was specifically designed to facilitate unidirectional flow of medicine.

**BEMA Potential Advantages**

- **ADHERES**
  - Bi-layered film technology
  - Mucoadhesive layer adheres to oral mucosa upon contact

- **DELIVERS**
  - Backing layer facilitates unidirectional flow across the oral mucosa, resulting in high bioavailability
  - Drug absorbed within minutes

- **DISSOLVES**
  - Patient is free to talk while the film completely dissolves
  - Pleasant taste
Advancing Buprenorphine Delivery

BUNAVAIL Buccal Film

- BUNAVAIL buccal film is a novel buprenorphine/naloxone product engineered to provide:
  - A patient-oriented medication interface
    - Easy to use
    - Pleasant tasting
    - May swallow and talk
    - Film adheres to inside of cheek in seconds
    - Discreet
  - Efficient delivery of buprenorphine to minimize opioid receptor binding in GI tract and opioid-induced constipation
    - Bioavailability = ~50% (vs ~25% for Suboxone sublingual tablet)


Newer Formulations of Buprenorphine

- Suboxone ® film (2/0.5 mg; 4/1 mg; 8/2 mg; and 12/3 mg)
- Buprenorphine (generic) tablets (2/0.5 mg and 8/2 mg)
- Zubsolv ® (usually 5.7 mg/1.4 mg tablet, placed under tongue; also in 1.4 mg/0.36 mg, 8.6 mg/2.1 mg, and 11.4 mg/2.9 mg tablets)
- Bunavail ® (2.1/0.3; 4.2/0.7; 6.3/1.0) – film placed inside the cheek (buccal)
- Probuphine ® implant (not for withdrawal mgmt.)
- Sublocade ® injectable (not for withdrawal mgmt.)
Opioid Withdrawal Management with buprenorphine products

- Confirm patient is in withdrawal (objective symptoms)
- Understand date of last dose, and the half-life of the agent last used
- Hold off on first buprenorphine dose to avoid INDUCED WITHDRAWAL
- First dose = 2 mg, and observe
- Total dose on day 1 = 8-12 mg of Suboxone product, or equivalent dose with other products

Opioid Withdrawal Management with buprenorphine products

What will happen?

- If there is precipitated withdrawal, it happens immediately upon absorption
- If not, relief also happens immediately
- Relief of symptoms may not be complete with 1st dose, so re-dose (every 1-2 hrs)
- Continue dosing to generate response (no OWS, cravings much diminished or eliminated)
Opioid Withdrawal Management with buprenorphine products

• DURATION OF BUPE?
  • Is this INDUCTION onto MAINTENANCE THERAPY?
  • Is this solely DETOX?

• “30-day detox” ??
• “6-day detox”

A pitch to all docs...

• Even YOU can be a “Suboxone doc”!
  • The ability to legally use buprenorphine products in addiction management and in **withdrawal management**; **though use for withdrawal management if “off label” since none of the manufactures applied for a label from the FDA**
  • To obtain the DEA waiver that allows you to prescribe buprenorphine for management of addiction or withdrawal, you need to be certified in addiction medicine or addiction psychiatry OR...take an 8 hour CME course (curriculum approved by the federal Center for Substance Abuse Treatment); these courses are on-line or live on-site trainings
  • Now APNPs and PA-Cs also; and residents too!
  • see www.asam.org or www(aaap.org
Opioid Withdrawal — the “Take Home”

- Patients’ worst nightmare – a major barrier to engagement in and initiation of treatment.
- “it doesn’t kill, you, just makes you wish you were dead…”
- Objective, subjective and protracted withdrawal.
- Many pain patients who never had true addiction can have terribly uncomfortable and protracted O.W.S. (including DA abstinence sx)

Opioid Withdrawal Management: Summary

- Replace opioid (if patient has physical dependence without addiction), then taper
- Opioid Detox with methadone (in OTPs only)
- Opioid Detox with buprenorphine
  (in any medical clinic, if CSAT-certified physician, DEA-waivered physician)
- Clonidine is still ‘standard treatment’, though bup is safe/effective/liked; and actually better
- Lofexidine will be used by some as “the only FDA approved non-opioid” product with a standard dosage recommendation (Lucemyra®)
Stimulants

- **Cocaine**
- **Amphetamines**
  - Methamphetamine
  - Dextroamphetamine
  - Amphetamine sulfate
- **Methylated amphetamines** (‘designer drugs’)
  - MDMA—Ecstasy
  - MDA, DOM, STP
- **Psychostimulants**
  -- Methylphenidate (Ritalin)
  -- Pemoline (Cylert)
- **Ephedrine/Pseudoephedrine**
- **Phenylpropanolamine**
- **Amphetamine Congeners**
  - Benzphetamine
  - Diethylpropion
  - Fenfluramine
  - Phentermine
  - Phenmetrazine
  - Phendimetrazine
  - Mazindol

Cocaine Withdrawal

- **Phase one – Crash**
  - Initial - Intense dysphoria & craving
  - Middle – Desire to sleep, dysphoria, may start to use other substances or pursue supplies
  - Late – Hypersomnia and increased appetite – lasts 3 to 4 days
- **Phase two – Withdrawal**
  - Honeymoon – 12 hours to 4 days – reduced craving, improved mood and sleep pattern
  - Dysphoria – depression, lethargy, anhedonia, reemergence of craving – lasts 6 to 18 weeks
- **Phase three – Extinction**
  - Gradual improvement of mood, ability to experience pleasure, & interest in environment – lasts months
Stimulant Detox
(Stimulant Replacement?)

• Replacement, stabilization, and graded step-wise reduction is **not recommended** for cocaine, amphetamine, psychostimulant (Ritalin, Adderal, Cylert), or ‘designer drug (MDMA, ‘Ecstasy’) users
• Replacement, etc., is useful for persons with caffeine addiction (switch to oral tablets, decrease by 10% per day)

Management of Cocaine Withdrawal

• Phase I: bromocryptine ????

• Phase III: desipramine ????
Hallucinogen Detox
(Social Detox)

• Replacement strategies do not apply
• The problem isn’t ‘withdrawal’, it’s intoxication, with subsequent anxiety/panic in the wake of unanticipated dissociative symptoms
• ‘Talk Down’ the person on a ‘bad trip’ with psilocybin, LSD, hashish (esp. oral THC)
• ‘Talking Down’ often insufficient for ‘trips’ on PCP or Jimson weed (*Datura stramonium*)

Nicotine Detox
Nicotine Replacement Therapy--NRT

• Transdermal
• Oral (buccal)
• Nasal
• Inhaled
NRT

- Nicotine Patch
  - 1 mg for each cigarette smoked (tolerance level)
  - 7 mg, 14 mg, 21 mg, two 14’s = 28, two 21’s = 42
- Nicotine “gum” and lozenge
  - 2 mg every 2 hours – if smoking 1 ppm or less
  - 4 mg every 2 hours – if smoking 2 ppm or thereabouts
- Addiction Management = best results from combination of both
- Withdrawal Management is the foundation of Addiction Management w.r.t. addiction involving nicotine use, since #1 driver of return to use/continued use/inability to abstain is negative reinforcement from the drug nicotine (a drive to remove the negative feelings from NWS)

NRT

- Instruction in how to use the products is a key to success
- Do not use “like gum” – do not swallow saliva right away
- Generate nicotine in the oral cavity and wait 30” and feel the tingling in your mouth; allow it to be absorbed through lining of oral cavity
- Keep pH of oral cavity basic (ionized molecules cross biological membranes poorly, and “basic” nicotine is ionized by “acidic” agents
  - Citric acid, carbonic acid, tannic acid

  And contrary to initial teachings and lingering tradition, it is safe and proper to prescribe these agents for persons still smoking.
The ASAM Criteria
(2013 edition)

The ASAM Criteria

• Intensity of Service should derive from Severity of Illness
• Treatment should follow multidimensional Assessment
• Diagnosis—Treatment Plan—Determination of Level of Care
Assessment Dimensions

• Intoxication/Withdrawal Potential
• Biomedical Conditions/Complications
• Emotional/Behavioral/Cognitive Conditions
• Treatment Acceptance/Readiness/Motivation
• Relapse/Continued Use Potential
• Recovery Environment

Levels of Care for Specialty Treatment

• 0.5 Screening/Brief Intervention/Education
• 1.0 General Outpatient
• 2.0 Intensive Outpatient/Partial Hospital
• 3.0 Medically Monitored/Residential halfway houses, extended care, TC’s
• 4.0 Medically Managed/Inpatient
Levels of Care for Withdrawal Management and Intoxication Management

WM 1.0 General Outpatient
WM 2.0 Intensive Outpatient/Partial Hospital

Level 3.2 WM: Clinically Managed Residential Withdrawal Management
Level 3.7-WM: Medically Monitored Inpatient Withdrawal Management

Level 4-WM: Medically Managed Intensive Inpatient Withdrawal Management

Addressing Withdrawal Management and Intoxication Management

The ASAM Criteria describes various levels of care for withdrawal management for adults as if these services were offered separately from whatever services a patient may need to manage their addiction (substance use disorder).

In many cases, services for withdrawal management and services for addiction management are offered concurrently, by the same staff, in the same treatment setting, in an integrated manner. But in making decisions about the clinical necessity of offering specific interventions to address intoxication or withdrawal, The ASAM Criteria “unbundles” services (at least conceptually) and examines the features of a patient’s clinical presentation which may indicate specific interventions for “detoxification” – now termed “withdrawal management.”

The widely used general term of “detoxification” can involve management of intoxication episodes and withdrawal episodes. Adults, at various points in time, may be in need of intoxication management and may be in need of withdrawal management, in addition to management of their substance use disorder. Adolescents are more frequently in need of management for intoxication episodes than management for withdrawal syndromes.
The process of withdrawal management includes not only attenuation of the physiological and psychological features of withdrawal, but also interrupting the momentum of habitual compulsive use in persons with addiction. Thus, a person admitted for withdrawal management is also receiving professional services that can serve to “break the cycle” of use and enable the patient to establish the first day(s) of abstinence and to be evaluated for the need for further care. The time spent in withdrawal management is a time of critical importance for initial engagement in addiction management services when treatment for a diagnosed substance use disorder or gambling disorder is indicated. Because of the force of the momentum of habitual compulsive use and the difficulties inherent in overcoming it (even when there is no clear physiological withdrawal syndrome per se), this phase of treatment often requires a greater intensity of services to establish initial treatment engagement and patient role induction.

Introduction to Withdrawal Management

When a person’s substance use disorder has progressed to the point that physical dependence has developed, withdrawal management becomes the first (but not the sole) priority in treatment planning. The onset of a physical withdrawal syndrome, uncomfortable and potentially dangerous, arguably provides an unparalleled opportunity to engage a patient in what will hopefully be sustained recovery. Because current withdrawal management protocols can relieve withdrawal symptoms so quickly and effectively, counseling and therapy focused on initiation or resumption of recovery can be instituted at the same time as withdrawal management, rather than being delayed.

Although withdrawal management has historically been considered an inpatient procedure, current medication protocols now allow all but the most severe withdrawal syndromes to be managed effectively on an ambulatory basis. One great advantage of the ambulatory setting is that the simultaneous engagement in ongoing recovery treatment is much more feasible than when the withdrawal is managed in a general hospital where other addiction-specific services are not offered.
Health maintenance and population health management require that health care providers attend not only to stabilizing and resolving acute symptoms, but also to minimizing the potential for readmission to intensive levels of service, such as re-hospitalizations.

Put another way, a “successful detox” encounter involves more than acute management of withdrawal. It involves engagement in services to address the accompanying addiction process and thus reduce the likelihood of “readmission for detox.” Integrated systems of care which are accountable (financially and otherwise) for health outcomes will be highly motivated to use the withdrawal management encounter as an opportunity to identify cases of addiction that need to be treated and otherwise may have escaped identification.

Withdrawal management of some patients can be carried out in the office (Level 1-WM) or in more structured outpatient settings (Level 2-WM) without the use of beds or intensive nursing monitoring.

Intensive medical monitoring is required for Level 2-WM because the patients are at risk rating scores of 2 and 3, indicating moderate to significant risk in withdrawal. Other patients may need to be monitored for a period of time before an appropriate determination can be made. (Such monitoring can, at times, be carried out in what is technically considered an outpatient setting, but may require an even more structured service, such as a “23-hour observation bed.”)

Some withdrawal management programs that are described as Level 3 may have the capacity for more or less intensive medical monitoring of withdrawal management. For example, Level 3.2-WM social setting withdrawal management may provide only minimal medical monitoring, while a Level 3.7-WM withdrawal management service includes significant medical monitoring.
The ASAM Criteria matches a patient’s severity of illness along Dimension 1 with five intensities of withdrawal management service: Level 1-WM, Level 2-WM, Level 3.2-WM, Level 3.7-WM, and Level 4-WM.

The qualifier “WM” designates a withdrawal management service within the broad division (such as Level 3.2-WM, Clinically Managed Residential Withdrawal Management services or Social Setting Withdrawal Management).

In the adult criteria, a particular withdrawal management service can be provided separately (“unbundled”) from other treatment services. When such services are provided separately, a sufficiently comprehensive biopsychosocial screening assessment and linkage to addiction management services is essential to avoid the circumstance in which patients revolve through acute care facilities in repeated cycles of acute stabilization and relapse (the “revolving door syndrome”).

Variable Withdrawal Risk Assessment Matrix

Alcohol use leads to physical dependence in a minority of people with alcohol use disorder, but the widespread use of alcohol makes alcohol withdrawal syndrome (AWS) the most commonly seen withdrawal syndrome. Careful monitoring is required because of the possibility of grand mal seizures or alcohol withdrawal delirium.

Risk Factors of concern:
- A past history of seizures or delirium tremens
- Frequent sleep disturbances or nightmares in the previous week
- The presence of sweating, tremor, or a pulse over 100 while the blood alcohol level is over .10 mg%
- Severe somatic disease, particularly infection

The CIWA-Ar scale can be a useful tool, but it has only been validated for tracking the withdrawal management process— not for making level of care decisions. Because it does not take into account the influence of the other five ASAM criteria dimensions, it should only be used as part of the decision-making process and not as a stand-alone determinant for level of care decisions. Studies have documented its misapplication when the elevated CIWA-Ar score is in fact due to a delirium with an etiology other than AWS, resulting in the actual disorder going untreated.
Thank you!

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