‘Complicated Withdrawal’

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Disclosures: Shamim Nejad, MD

“Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.”
Complicated Withdrawal: Overview

- Epidemiology
- Complicated alcohol withdrawal syndrome (AWS)
  - Signs and symptoms
  - Pathophysiology
  - Management strategies
Phenotypes of AWS

• 4 main clinical states:
  – Autonomic hyperactivity
  – Neuronal excitation
  – Hallucinations (+/- paranoid state)
  – Alcohol withdrawal delirium (*delirium tremens*)

• Uncomplicated AWS
• Complicated AWS
  • Alcoholic hallucinosis
  • Alcohol related seizures
  • Alcohol withdrawal delirium

<table>
<thead>
<tr>
<th>Stages</th>
<th>Clinical Findings</th>
<th>Onset (Usual*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early or Uncomplicated</td>
<td>1) Anxiety, <strong>fine</strong> tremor (anxiety), tachycardia (anxiety); headache; palpitations; anorexia; GI upset; general malaise 2) May have elements of catacholamine excess (slight coarse tremor, elevated BP, elevated HR, diaphoresis, slight fever)</td>
<td>6-36 hrs</td>
</tr>
<tr>
<td>Alcoholic Withdrawal Seizure</td>
<td>Generalized, tonic-clonic seizures, status epilepticus (rare)</td>
<td>6-48 hrs</td>
</tr>
<tr>
<td>Alcoholic Hallucinosis</td>
<td>Visual, auditory, and/or tactile hallucinations</td>
<td>12-48 hrs</td>
</tr>
<tr>
<td>Alcoholic Withdrawal Delirium</td>
<td>Delirium, tachycardia, hypertension, agitation, fever, diaphoresis, <strong>coarse</strong> tremor</td>
<td>48-96 hrs</td>
</tr>
</tbody>
</table>
Neurotransmitters: GABA and Glutamate
GABA and Glutamate – Intermittent Alcohol Use

Baseline Activity

GABA activity

Glutamate activity
GABA and Glutamate – Acute Alcohol Use

Ethanol acting on GABA receptor

Baseline Activity

GABA activity

Glutamate activity
GABA and Glutamate – Chronic Alcohol Use

Ethanol acting on GABA receptor

Original Baseline Activity

New Baseline Activity

GABA activity

Glutamate activity
GABA and Glutamate – Abrupt Cessation of Alcohol

Baseline Activity

GABA activity

Glutamate activity

Amount of GABA agonism needed to override glutamate activity
Neurotransmitter Dysfunction in AWS – Uncomplicated Withdrawal

↓GABA Activity + ↑Glutamate Activity

↑Noradrenergic Activity

(+)

↑Dopamine Release

↓

Uncomplicated Alcohol Withdrawal

↑

Complicated Alcohol Withdrawal

Neurotransmitter Dysfunction in AWS – Alcohol Withdrawal Seizure

↓GABA Activity + ↑Glutamate Activity

↑Noradrenergic Activity

(+)

(+)

↑Dopamine Release

Uncomplicated Alcohol Withdrawal

Complicated Alcohol Withdrawal

Neurotransmitter Dysfunction in AWS – Alcoholic Hallucinosis

↓GABA Activity + ↑Glutamate Activity

(++)

↑Noradrenergic Activity

(+)

↑Dopamine Release

↓GABA Activity ↓GABA Activity

↓GABA Activity

↓GABA Activity

Uncomplicated Alcohol Withdrawal

Complicated Alcohol Withdrawal

Neurotransmitter Dysfunction in AWS – Alcohol Withdrawal Delirium

- **↓GABA Activity** + **↑Glutamate Activity** → **↑Noradrenergic Activity** → **↑Dopamine Release**

  - **Uncomplicated Alcohol Withdrawal**
  - **Complicated Alcohol Withdrawal**

**Clapp, P. et al.** How Adaptation of the Brain to Alcohol Leads to Dependence: A Pharmacological Perspective. Alcohol Research and Health Vol. 31, 2008; Pages 310–339.

www.mghcme.org
Management of AWD

- **Supportive Care**

- **Wernicke’s Treatment/Prophylaxis**
  - Signs: thiamine 500mg IV TID
  - Risk: thiamine 100mg IV/IM BID

- **Pharmacologic management**
  - Benzodiazepines
    - Antiepileptic drugs (AEDs)
    - Ethanol
    - Dexametomidine
    - Propofol

- **BZD Administration Strategies**
  - Prophylaxis
    - Front-loading
    - Fixed dose
  - Active Symptoms
    - Symptom Triggered
    - Fixed schedule + PRN

- **Augmentation agents**
  - Beta Blockers
  - Clonidine
  - Haloperidol
AWS Treatment Algorithm

Uncomplicated AWS

- Normal Mental Status
  - CIWA (or other STP)

- Delirious or high delirium risk/History of Complicated AWS
  - Fixed-Dose BZD or Phenobarbital Protocol

Complicated AWS
Rating Scales in AWS

- CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol – Revised)
- AWS (Alcohol Withdrawal Symptoms rating scale)
- SAWS (Short Alcohol Withdrawal Scale)
- SAS (Severity Assessment Scale)
Symptom-Triggered Protocols: CIWA

**CIWA-Ar**

- Used to guide AWS management strategies
  - Relatively easy to use
  - Reliable and validated assessment tool – for non-medically/surgically ill
  - Scores correlate with severity of AWS - for non-medically/surgically ill
  - NOT diagnostic ---- it is an ASSESSMENT TOOL
  - Inter-rater reliability only fair to poor

- CIWA-Ar
  - Nausea and Vomiting
  - Tremor
  - Paroxysmal Sweats
  - Anxiety
  - Agitation
  - Tactile Disturbances
  - Auditory Hallucinations
  - Visual Disturbances
  - Headache, ‘fullness in head’
  - Orientation, clouding of sensorium
# CIWA-Driven BZD-Based

## Disease-Specific Medications
### CIWA-Driven Benzodiazepine-based Alcohol Detox

**LORazepam (ATIVAN)** is the suggested medication for EtOH detox on med/surg units.

<table>
<thead>
<tr>
<th>CIWA-driven benzodiazepine detox guidelines</th>
<th>Use with caution in patients</th>
<th>Avoid in patients</th>
<th>Contraindicated in patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appropriate for patients:</strong></td>
<td>1. Younger than 18 years old</td>
<td>1. With history of delirium tricums</td>
<td>1. With active DTs or severe withdrawal symptoms not responding to benzodiazepines</td>
</tr>
<tr>
<td>2. Not already in severe withdrawal</td>
<td>2. With history of sedative/hypnotic abuse</td>
<td>2. With history of alcohol withdrawal seizures</td>
<td>2. With altered mental status and/or delirium</td>
</tr>
<tr>
<td>3. Not showing evidence of delirium</td>
<td>3. With toxic DIL</td>
<td>3. With history of benzodiazepine non-response or benzodiazepine resistance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4. Using clonidine or beta-blockers</td>
<td>4. With history of previous ICU admission for alcohol detox</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5. At risk for paradoxical disinhibition with benzodiazepines</td>
<td>5. Showing current symptoms of delirium's encephalopathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Acute and chronic TBI</td>
<td>6. With respiratory compromise or at risk for respiratory compromise</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Neurodegenerative disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>c. History of alcohol related blackouts and/or assaultsive behavior</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

When the patient's vital signs and withdrawal symptoms have been stable for 24 hours, initiate the standing taper orders with the same benzodiazepine medication using the 'alcohol withdrawal standing taper instructions post 24 hours order panel'.

- **Lorazepam (ATIVAN) Oral - CIWA Driven**
  - 0.4 mg, Oral. Every 4 hours PRN, withdrawal signs/symptoms. CIWA less than 9 = no medication needed. Continue administering CIWA every 4 hours. Stop CIWA after 6 consecutive scores less than 5. CIWA 9 to 15 = 2 mg Continue CIWA every 4 hours. If no improvement in CIWA after 2 consecutive dosings or if patient shows worsening of symptoms, contact RC to change regimen. CIWA 16 to 20 = 4 mg Contact RC to change regimen. Repeat CIWA in 2 hours. CIWA greater than 20 = 4 mg Contact RC. Switch to standing dose regimen.

- **Lorazepam (ATIVAN) injection - CIWA Driven**
  - 0.4 mg, Intravenous. Every 4 hours PRN, withdrawal signs/symptoms. CIWA less than 9 = no medication needed. Continue administering CIWA every 4 hours. Stop CIWA after 6 consecutive scores less than 5. CIWA 9 to 15 = 2 mg Continue CIWA every 4 hours. If no improvement in CIWA after 2 consecutive dosings or if patient shows worsening of symptoms, contact RC to change regimen. CIWA 16 to 20 = 4 mg Contact RC to change regimen. Repeat CIWA in 2 hours. CIWA greater than 20 = 4 mg Contact RC. Switch to standing dose regimen.

- **Diazepam (VALIUM) Oral - CIWA Driven**
  - 0.20 mg, Oral. Every 4 hours PRN, withdrawal signs/symptoms. CIWA less than 9 = no medication needed. Continue administering CIWA every 4 hours. Stop CIWA after 6 consecutive scores less than 5. CIWA 9 to 15 = 10 mg Continue CIWA every 4 hours. If no improvement in CIWA after 2 consecutive dosings or if patient shows worsening of symptoms, contact RC to change regimen. CIWA 16 to 20 = 20 mg Contact RC to change regimen. Repeat CIWA in 2 hours. CIWA greater than 20 = 50 mg Contact RC. Switch to standing dose regimen.

- **Chlordiazepoxide (LIBRUM) capsule** (Avoid on med/surg units. DO NOT USE for detox from other benzodiazepines)
  - 0.50 mg, Oral. Every 4 hours PRN, withdrawal signs/symptoms. CIWA less than 9 = no medication needed. Continue administering CIWA every 4 hours. Stop CIWA after 6 consecutive scores less than 5. CIWA 9 to 15 = 25 mg Continue CIWA every 4 hours. If no improvement in CIWA after 2 consecutive dosings or if patient shows worsening of symptoms, contact RC to change regimen. CIWA 16 to 20 = 50 mg Contact RC to change regimen. Repeat CIWA in 2 hours. CIWA greater than 20 = 50 mg Contact RC. Switch to standing dose regimen.
CIWA-Ar: Things To Consider

- Patient Location
- Mental status
- Level of medical comorbidity
- Current severity of alcohol withdrawal
- History of repeated complicated alcohol withdrawal

When used, remember that Epic or any protocol order set(s) are only a ‘starting point,’ and you may need to adjust dose and route to be relevant to your patient.

- Alternative protocol should be available if there are contraindications to CIWA-Ar use
Complicated AWS: Fixed-Dose

Standing Regimen Benzodiazepine-based Alcohol Detox

**LORazepam (ATIVAN)** is the suggested medication for EtOH detox on med/surg units.

<table>
<thead>
<tr>
<th>Fixed-dose benzodiazepine detox guideline</th>
<th>Use with caution in patients:</th>
<th>Avoid in patients:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider for patients:</td>
<td>1. Polypathy</td>
<td>1. With respiratory compromise or at risk for respiratory compromise</td>
</tr>
<tr>
<td>1. For whom CIWA is contraindicated</td>
<td>2. With active DT's or severe withdrawal symptoms not responding to benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>2. With CIWA score is greater than 16</td>
<td>3. With history of alcohol withdrawal seizures</td>
<td></td>
</tr>
<tr>
<td>3. With history of delirium tremens</td>
<td>4. With history of benzodiazepine non-response or benzodiazepine resistance</td>
<td></td>
</tr>
<tr>
<td>4. With history of benzodiazepine resistance</td>
<td>5. With altered mental status and/or high risk for delirium</td>
<td></td>
</tr>
<tr>
<td>5. With history of benzodiazepine non-response or benzodiazepine resistance</td>
<td>6. With history of benzodiazepine non-response or benzodiazepine resistance</td>
<td></td>
</tr>
<tr>
<td>6. With history of previous ICU admission for alcohol detox</td>
<td>7. With history of previous ICU admission for alcohol detox</td>
<td></td>
</tr>
</tbody>
</table>

Avoid in patients:

- Acute and chronic TBI
- Neurodegenerative disorders
- History of alcohol related black-outs and/or aggressive behavior

When the patient’s vital signs and withdrawal symptoms have been stable for 24 hours, initiate the standing taper orders with the same benzodiazepine medication using the 'alcohol withdrawal standing taper instructions post 24 hours order panel'.

- **LORazepam (ATIVAN) Oral Standing Regimen**
  - 2 mg, Oral, Every 4 hours
  - Standing regimen benzodiazepine-based alcohol detox. 1) Continue standing dose until vital signs and withdrawal symptoms have been stable for 24 hours. 2) Hold for acute onset of benzodiazepine intoxication, including: sedation, dizziness, ataxia, slurred speech, disorientation or delirium.
  - If patient exhibits no signs of alcohol withdrawal (stable vital signs, no tremors, no agitation), and contact RC to begin lorazepam taper. 4) Notify RC if no improvement after two consecutive doses or worsening of symptoms.

- **PRN LORazepam (ATIVAN) tablet**
  - 1 mg, Oral, Every 1 hour PRN, withdrawal signs/symptoms. If two PRN doses are given, contact RC to consider changing standing regimen and to assess for benzodiazepine intoxication.

- **LORazepam (ATIVAN) Injection Standing Regimen**
  - 2 mg, Intravenous, Every 4 hours
  - Standing regimen benzodiazepine-based alcohol detox. 1) Continue standing dose until vital signs and withdrawal symptoms have been stable for 24 hours. 2) Hold for acute onset of benzodiazepine intoxication, including: sedation, dizziness, ataxia, slurred speech, disorientation or delirium. 3) Hold if patient exhibits no signs of alcohol withdrawal (stable vital signs, no tremors, no agitation), and contact RC to begin lorazepam taper. 4) Notify RC if no improvement after two consecutive doses or worsening of symptoms.

- **PRN LORazepam (ATIVAN) Injection**
  - 1 mg, Intravenous, Every 1 hour PRN, withdrawal signs/symptoms. If two PRN doses are given, contact RC to consider changing standing regimen and to assess for benzodiazepine intoxication.

- **Diazepam (VALIUM) Oral Standing Regimen**
  - 10 mg, Oral, Every 4 hours
  - Standing regimen benzodiazepine-based alcohol detox. 1) Continue standing dose until vital signs and withdrawal symptoms have been stable for 24 hours. 2) Hold for acute onset of benzodiazepine intoxication, including: sedation, dizziness, ataxia, slurred speech, disorientation or delirium. 3) If patient exhibits no signs of alcohol withdrawal (stable vital signs, no tremors, no agitation), and contact RC to begin diazepam taper. 4) Notify RC if no improvement after two consecutive doses or worsening of symptoms.

- **PRN Diazepam (VALIUM) tablet**
  - 5 mg, Oral, Every 1 hour PRN, withdrawal signs/symptoms. If two PRN doses are given, contact RC to consider changing standing regimen and to assess for benzodiazepine intoxication.

- **Chlordiazepoxide (LIBRUM) Oral Standing Regimen**
  - [Avoid on med/surg units. DO NOT USE for detox from other benzodiazepines]
  - 50 mg, Oral, Every 4 hours
  - Standing regimen benzodiazepine-based alcohol detox. 1) Continue standing dose until vital signs and withdrawal symptoms have been stable for 24 hours. 2) Hold for acute onset of benzodiazepine intoxication, including: sedation, dizziness, ataxia, slurred speech, disorientation or delirium. 3) Hold if patient exhibits no signs of alcohol withdrawal (stable vital signs, no tremors, no agitation), and contact RC to begin chlordiazepoxide taper. 4) Notify RC if no improvement after two consecutive doses or worsening of symptoms.

- **PRN Chlordiazepoxide (LIBRUM) capsule**
  - [Avoid on med/surg units. DO NOT USE for detox from other benzodiazepines]
  - 25 mg, Oral, Every 1 hour PRN, withdrawal signs/symptoms. If two PRN doses are given, contact RC to consider changing standing regimen and to assess for benzodiazepine intoxication.
AWS Treatment Algorithm

Uncomplicated AWS

- Normal Mental Status
  - CIWA (or other STP)

- Delirious or high delirium risk/History of Complicated AWS
  - Fixed-Dose or Phenobarbital Protocol

Complicated AWS

- Non-ICU
  - Fixed-Dose or Phenobarbital Protocol

- ICU
  - Phenobarbital Protocol
  - Dexmedetomidine
  - BZD Symptom-Triggered Protocol (RASS)
Non-BZD Based Strategies

• Anti-epileptic Drugs:
  – Valproate
  – Carbamazepine
  – Phenobarbital

• Alpha agonists
  – Dexmedetomidine
# Phenobarbital for Treatment of AWS

<table>
<thead>
<tr>
<th>Reference</th>
<th>Pts. (N)</th>
<th>AWS Severity</th>
<th>Control</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosenson (2013)</td>
<td>102</td>
<td>Unknown</td>
<td>Lorazepam +/- placebo</td>
<td>Level of admission LOS Adverse events</td>
<td>Decreased ICU admissions Decreased LOS None</td>
</tr>
<tr>
<td>Hendey (2011)</td>
<td>44</td>
<td>Moderate</td>
<td>Lorazepam</td>
<td>Change in CIWA-Ar Score upon ED disposition</td>
<td>Difference not significant</td>
</tr>
<tr>
<td>Young (1987)</td>
<td>62</td>
<td>Moderate</td>
<td>None</td>
<td>Seizures (n) Delirium (n) Discharge from ED (%)</td>
<td>0 4 92%</td>
</tr>
<tr>
<td>Ives (1991)</td>
<td>+70</td>
<td>Unknown</td>
<td>None - observational noncomparative report</td>
<td>Seizures (%) Delirium (%)</td>
<td>No ‘undue consequences’</td>
</tr>
<tr>
<td>Rosenthal (1998)</td>
<td>32</td>
<td>Mild-moderate</td>
<td>Valproate</td>
<td>MSSA Score Phenobarbital Dose (n)</td>
<td>Change not significant VPA: 20 Control: 39 p&lt;0.05</td>
</tr>
<tr>
<td>Mariani (2006)</td>
<td>27</td>
<td>Moderate</td>
<td>Gabapentin</td>
<td>Change in CIWA-Ar Score Phenobarbital Doses (n)</td>
<td>Difference not significant Gabapentin: 8 Phenobarbital: 5 p&lt;0.45</td>
</tr>
</tbody>
</table>
Phenobarbital: Mechanism of Action


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Phenobarbital

• Has GABA agonism AND decreases glutamate activity
• Research does not demonstrate decreased BZD receptor sensitivity as seen with benzodiazepines
• Minimal changes in mental status and no observed paradoxical disinhibition
• Pharmacokinetics are reliable
  ▪ Able to target specific serum levels (which are meaningful clinically)
  ▪ Does NOT have a narrow therapeutic index
  ▪ Longer-acting

Complicated AWS: Phenobarbital Protocol

**Risk Factors for Alcohol Withdrawal Delirium**

- History of past seizure or delirium tremens
- Seizure in the field or in ED prior to admission
- Acute concurrent medical illness
- More days since last drink (2 or more days)
- Elevated admission blood alcohol
- Heavier and longer drinking history
- Signs of autonomic hyperactivity with BAL of > .1g/dL
- AGE>40
- Burn related injuries
- Falls, particularly with long bone fractures
- Elevated MCV, AST (? CDT)
- On one study – MVA had negative predictive value

Complicated AWS: Phenobarbital Protocol

- **High Risk:**
  - Past DTs +/- Past seizures AND
    - + Recent alcohol use (≥2 weeks) or
    - Active symptoms of AWS or
    + Recent alcohol use, + BAL, elevated MCV, elevated AST:ALT ratio

- **Medium Risk (active alcohol use disorder plus 2 of the following):**
  - More days since last drink (2 or more days)
  - Elevated BAL on admit
  - Autonomic dysfunction with BAL > .1 g/dL
  - Elevated MCV and/or AST:ALT ratio
  - Heavier and longer drinking history
  - AGE > 35
  - Burn related injuries
  - Falls, particularly with long bone fractures

- **Risk of Sedation:**
  - Age ≥65 years old
  - Hepatic dysfunction
  - Opiate administration
  - Head injury – neuro checks
  - Recent administration of BZDs
  - Current administration of sedatives

- **Respiratory Compromise:**
  - PNA
  - Rib fractures
  - Chest tube(s)
  - Pulmonary contusion(s)
  - C-collar/brace

Risk of Alcohol Withdrawal Delirium

High Risk of AWD

- Minimal or No Risk of Respiratory Compromise
  - 12-15mg/kg

- + Risk of Sedation or Respiratory Compromise
  - 10-12mg/kg

- + Severe Risk of Sedation or Respiratory Compromise
  - 6-10mg/kg

Medium Risk of AWD

- Minimal or No Risk of Respiratory Compromise
  - 10-12mg/kg

- + Risk of Sedation or Respiratory Compromise
  - 8-10mg/kg

- + Severe Risk of Sedation or Respiratory Compromise
  - 6-8mg/kg

Low Risk of AWD: Use PRN BZDs cautiously

Nejad et al., *J of Trauma*, in preparation

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Complicated AWS: Phenobarbital Protocol

- Calculate target loading dose with phenobarbital depending on alcohol use severity and comorbid medical illness

- IBW x (6 to 15mg/kg) = total mg (of loading dose)

- Where:
  - IBW for men is: 50 + 2.3 kg/inch over 5 feet.
  - IBW for women is: 45.5 + 2.3kg/inch over 5 feet.

- Give loading dose intramuscularly:
  - 40% of loading dose given immediately
  - 30% of loading dose given 3 hours after 1st IM administration
  - 30% of loading dose given 3 hours after 2nd IM administration
  - Serum phenobarbital level should be checked 5 hours after the 3rd IM administration

Nejad et al., *J of Trauma*, in preparation
Complicated AWS: Phenobarbital Protocol

- On day 2, start maintenance dose:

\[ MD = \frac{(Cl) \times (CPss) \times (T)}{(S) \times (F)} \]

- Where:
  - MD: maintenance dose
  - Cl: rate of clearance (0.096 L/day/kg)
  - CPss: desired steady state serum level (10-20 ug/mL)
    - If initial target level 15, then use 20ug/mL
    - If initial level 12, then use 15ug/mL
    - If initial level 10, then use 12ug/mL
    - If initial level 8, then use 10ug/mL
    - If initial level 6, then use 10ug/mL
  - S: Fraction of the total molecular weight of active drug in salt form
  - F: Bioavailability

Therefore:

\[ \frac{0.096L/day/kg \times IBW (in Kg) \times (10-20ug/mL)(1 \text{ day})}{(1.0) \times (1.0)} = \text{Total maintenance dose} \]

- Maintenance dose is given ORALLY (or IM) and split in ½, given BID.
Complicated AWS: Phenobarbital Protocol

• Day 3 is the same as day 2
• Day 4 the oral dose is decreased by 50%
• Day 5 it stays the same
• Day 6 decrease 50%
• Day 7 decrease 50%
• Then discontinue

• No benzodiazepines allowed and an order is placed that none can be given to the patient

• Contraindications: acute intermittent prophyria, active/previous history of SJS/TEN or rash with AEDs

Nejad et al., J of Trauma, in preparation
<table>
<thead>
<tr>
<th>Clonidine</th>
<th>Dexmedetomidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Selectivity: $\alpha_2:\alpha_1$ 200:1</td>
<td>• Selectivity: $\alpha_2:\alpha_1$ 1620:1</td>
</tr>
<tr>
<td>• $t_{1/2} \beta$ 8 hrs</td>
<td>• $t_{1/2} \beta$ 2 hrs</td>
</tr>
<tr>
<td>• PO, patch, epidural</td>
<td>• Intravenous</td>
</tr>
<tr>
<td>• Antihypertensive</td>
<td>• Sedative-analgesic</td>
</tr>
<tr>
<td>• Analgesic adjunct</td>
<td>• Primary sedative</td>
</tr>
<tr>
<td>• IV formulation not available in US</td>
<td>• Only IV $\alpha_2$ available for use in the US</td>
</tr>
</tbody>
</table>
Complicated AWS: Dexmedetomidine

- Administer as a continuous IV infusion in the range of 0.2 to 1.4 µg/kg/h
  - Start at 0.2mcg/kg for one hour and ensure no bradycardia or hypotension, then titrate to need
  - *Almost no patient requires more than 0.6mcg/kg/hr for AWS*

- If hypotension develops give IVF bolus and rechallenge

- Avoid loading dose

- Normal response to vasoactive drugs
- Decreases oxygen consumption
- No effect on ICP
- Attenuates stress response
- Decreases metabolism
- Endocrine
  - ↓ NE release
  - ↓ insulin release
  - ↓ cortisol release
  - ↑ GH release
Complicated AWS: Dexmedetomidine

- **Patient Selection**
  - ICU patient with:
    - High sympathetic activity
    - Agitated
    - With discomfort/pain symptoms
    - Cirrhosis with active alcohol withdrawal symptoms

**Caution**

- Low blood pressure
- Hypovolemic/shock/significant SIRS
- Conduction defects/bradyarrhythmias/poor ventricular function
Complicated AWS: BZD STP - ICU

FLOWCHART 1:
**ESCALATING PHASE**
- Begin clonidine 0.3 mg TID if patient can take PO.
- Administer haloperidol if QTc < 550 ms
- Continue escalating dose therapy until maximum dose of 80 mg has been given twice

FLOWCHART 1:
**SCARIFICATING PHASE**
- Administer diazepam (10 mg IV if receiving first dose, otherwise DOUBLE last dose up to max of 80 mg)
- Assess RASS every 20 minutes

MICU Alcohol Withdrawal Protocol

V2.0

Has patient already received two doses of 80 mg?
- No
- Yes: GO TO RESCUE PHASE (FLOWCHART #3)

Patient should be considered benzodiazepine resistant. Discontinue all benzodiazepines and consider alternatives. Patient should not receive further benzodiazepines unless necessary for other reasons.

Is RASS below +1 for one hour?
- No
- Yes: GO TO TAPERING PHASE

See flowchart #2. Once patients leave escalating phase they CANNOT return to it. Benzodiazepine dosages must continue to decrease from this point forward.
Complicated AWS: BZD STP - ICU

FLOWCHART 3: RESCUE PHASE
Patients can enter this phase if:
- They fail the max dose of 80 mg diazepam x2
- They exceed 400 mg total of diazepam
- Uncontrollable symptoms recur after patient is in tapering phase
- Ongoing symptoms >24 hours after beginning treatment

MICU Alcohol Withdrawal Protocol V2.0

Dexmedetomidine can be used for control of persistent symptoms or to facilitate extubation:
- Start infusion at 0.2 mcg/kg/hr
- Discontinue clonidine
- Titrate up as needed to achieve RASS 0 to +1
- When goal RASS achieve, titrate down every 2 hours as tolerated

Consider other etiologies for symptoms. Use other pharmacologic therapies such as haloperidol, clonidine, etc.

If patient requires intubation treat with propofol infusion. Discontinue infusion periodically to determine whether symptoms persist.
Summary

- Early in hospital course, utilize epidemiologic data to help guide risk assessment for development of complicated and uncomplicated alcohol withdrawal

- Active medical illness and PMH, along with current AWS and past detoxification history can help guide you to management strategy: CIWA vs fixed dose vs non-BZD protocols

- Use understanding of pathophysiology of AWS and current symptoms being observed to help guide augmentation strategies for more complicated alcohol withdrawal cases, particularly in those patient with concomitant active medical and surgical illness