ED Management of Alcohol Withdrawal Syndrome

Additional Clinical Guidance

- Alcohol use disorder (AUD) is treatable.
  - Pharmacotherapy is evidence-based.
  - Recovery often requires multiple treatment attempts.
- Stigma prevents help-seeking and worsens health outcomes.
  - Care teams must challenge biases to provide compassionate, evidence-based care.
  - Use non-stigmatizing, person-first language and trauma-informed care to promote engagement.

Assessment

- The **Richmond Agitation-Sedation Scale (RASS)** is used to assess level of agitation, alertness, and sedation. The scale ranges from +4 (very agitated) to -5 (very sedated), with 0 representing an alert and calm state. Therapeutic goal is RASS 0 to –1.
- Advantages of **RASS** over **CIWA-Ar** for assessing alcohol withdrawal:
  - RASS is a rapid, single-item scale that does not require patients to answer questions.
  - CIWA-Ar can only be used in awake and alert patients and takes longer to assess.
- CIWA-Ar may be used in addition or as an alternative.

Labs

- Phenobarbital has predictable, linear pharmacokinetics; thus, serum levels generally do not need to be checked when remaining within the recommended dose of no more than 20mg/kg/day. Seek expert consultation if you consider exceeding this dose. Toxicity occurs with plasma levels >40 mcg/mL.

Pharmacotherapy

- Phenobarbital is increasingly recommended over benzodiazepines to treat AWS; it is preferred because:
  - Studies comparing phenobarbital and benzodiazepine monotherapy have shown fewer ICU admissions from the ED and shorter hospital stays with fewer adverse events (physical restraints, intubation) after admission in those given phenobarbital over benzodiazepines.
  - Patients who receive phenobarbital are significantly less likely to return to the ED within 72 hours and have not been shown to experience more adverse events.
  - Phenobarbital affects both inhibitory (GABA) and excitatory (glutamate) neurotransmitters. Benzodiazepines potentiate the GABA receptor, which helps calm the patient, but have no effect on excitatory neurotransmitters, which can cause paradoxical agitation.

- Phenobarbital has a rapid onset (5-20 min) and loading doses have a predictable, linear relationship to serum levels, and its maximum sedating effect occurs within 15 minutes of IV administration. It also has a long half-life (approximately 100 hours) with active metabolites, self-titrating over 3-4 days. This means that clinicians will see the deepest sedation while the patient is in the emergency department, but the protection from withdrawal symptoms will last for days after discharge.
- Benzodiazepines may cause delirium and be misinterpreted as ongoing alcohol withdrawal.

- Diazepam (Valium) is preferred over chlordiazepoxide (Librium) in acute care settings because:
  - Diazepam can be given orally or IV with peak sedation within 30-45 minutes.
  - Use of chlordiazepoxide results in unpredictable levels of sedation due to delayed peak effect.
  - Diazepam has a longer half-life (30-56 hour) with active metabolites, so therapeutic effect is extended.
  - Patients who receive chlordiazepoxide often need a prescription to dose after discharge due to its shorter half-life (24-48 hours) and lack of active metabolites. After discharge, patients are at risk of oversedation if they combine chlordiazepoxide with alcohol.
- Multiple or uncertain toxidrome(s):
  - Benzodiazepines are the best first-line therapy when the diagnosis is unclear or multiple toxidromes (e.g., concurrent opioid and/or benzodiazepine withdrawal, stimulant intoxication, etc.) are present.

Pathophysiology

- Alcohol withdrawal syndrome (AWS) typically occurs within 1-3 days following abrupt cessation or considerable decrease in heavy, chronic alcohol use. AWS ranges from mild to severe and can be life threatening.
- AWS symptoms may include:
  - Autonomic: tachycardia, tachypnea, dilated pupils, elevated blood pressure, elevated body temperature, diaphoresis, nausea/vomiting, diarrhea.
  - Motor: tremor, seizures, ataxia, gait disturbances, hyperreflexia, dysarthria.
  - Psychiatric: irritability, anxiety, agitation, insomnia, delirium, disorientation, illusions, delusions, hallucinations, affect instability, disinhibition.
- Vitamin deficiency:
  - Patients are at high risk for thiamine (vitamin B1) and folate deficiency and should receive supplementation.
  - Thiamine supplementation prevents and treats Wernicke encephalopathy, which is life threatening.

- Electrolyte imbalance:
  - Hyponatremia is common, especially amongst those who drink beer. This can be repleted with isotonic fluids.
  - Hypokalemia is common and should be corrected.
  - Patients are at risk for hypokalemia, hypophosphatemia and refeeding syndrome, and metabolic acidosis/alcohol-related ketoacidosis.
- Severe/complicated AWS:
  - Severe AWS refers to seizures, autonomic dysfunction, delirium, and Wernicke encephalopathy.
  - Risk factors for severe withdrawal include history of severe AWS, medical comorbidities, and co-dependence on benzodiazepines.

ALCOHOL WITHDRAWAL SYNDROME (AWS)		
Presentation	**Timeline**	**Signs and Symptoms**
Initial withdrawal	Onset can occur 6-8 hours after last drink	• Increased body temperature, diaphoresis • Anxiety, insomnia • Tremor, headache • Nausea/vomiting • Tachycardia, hypertension, palpitations
Alcohol withdrawal hallucinations	12-24 hours after last drink	• Tactile hallucinations most common • Visual/auditory hallucinations possible • May/may not have other AWS symptoms • Normal mental status
Withdrawal seizures	12-48 hours after last drink	• Often occur early and when other symptoms are not severe • Generalized tonic-clonic • Typically isolated and brief with short postictal period *Note: 1/3 with seizures will progress to delirium*
Alcohol withdrawal delirium *(formerly delirium tremens)*	3 days after initial AWS symptoms; lasts 1-8 days	• Agitation, disorientation, hallucinations • Hyperthermia, diaphoresis • Tachycardia, hypertension

Wernicke encephalopathy **Neuropsychiatric emergency!**		• Altered mental status • Ataxia • Oculomotor abnormalities *Note: Urgent, high dose IV thiamine replacement necessary to avoid death/Korsakoff syndrome*
Wernicke-Korsakoff syndrome		Brain injury resulting in: • Memory and cognitive impairment • Disorientation • Behavioral changes *Note: Brain damage is largely irreversible*

Table adapted from Gottlieb, et. al (2024) and Canver et. al (2024).

Special populations

- Phenobarbital is contraindicated in pregnancy.

Patient safety

- Monitor and maintain adequate fluid intake and electrolyte balance.
- Ensure thiamine and folate supplementation for all AWS patients.
- If a patient is at risk for or experiencing severe AWS, administer indicated medications immediately to prevent complications.
- Patients with symptoms **of Wernicke's encephalopathy must be urgently treated with IV thiamine.**

Discharge planning

- Arrange transfer to withdrawal management facility for ongoing management, if indicated/preferred by patient.
- Help the patient schedule a follow up appointment with primary care.
  - Ask the patient if they have an established provider and where they want to receive ongoing care.
  - Assist the patient with scheduling appointments and addressing barriers, like transportation. Refer to social work, if available.
  - Outpatient and inpatient/residential treatment programs can be found on the Department of Health's **Behavioral Health Agency Greenbook**.

- Discharge medications for AWS:
  - Most patients who receive diazepam or phenobarbital will not require a prescription for medications to treat ongoing AWS symptoms after discharge.
  - If the patient feels they need medications after discharge, consider gabapentin (first-line) or chlordiazepoxide (second-line):
    - Gabapentin 600mg TID
      - Gabapentin is preferred over a benzodiazepine due to less sedation risk.
      - Patient should have normal GFR and be under 65 years old.
      - Patient may continue this medication long term for management of AUD. See **Medications for Alcohol Use Disorder**.
      - If patient chooses not to continue gabapentin long term, advise against abrupt discontinuation due to seizure risk. Consider the following taper:
        - Gabapentin 300 mg tabs
        - Day 1: 1 tab every 6 hours
        - Day 2: 1 tab every 8 hours
        - Day 3: 1 tab every 12 hours
        - Day 4: 1 tab
        - May have one additional tab every 12 hours as needed x 5
        - Dispense #15
    - Chlordiazepoxide
      - Note delayed peak sedation and risk of oversedation if combined with alcohol. Discuss the risks and explain that the medication must not be combined with alcohol or other sedating substances.
      - Chlordiazepoxide is preferred over diazepam when unobserved because it is less sedating.
      - Prescribe:
        - Day 1: 50mg every 6 hours
        - Day 2: 25mg every 6 hours
        - Day 3: 25mg every 12 hours
        - Day 4: 25mg at night
        - Dispense #15, no refills
        - Do not use if consuming alcohol or taking other sedatives

- Offer medications to treat alcohol use disorder. See **Medications for Alcohol Use Disorder**.
- Provide naloxone for patients that use any street drugs and discuss safer use strategies, including not using alone.

Patient Education

Educate patients on:

- Strategies to reduce the harms of alcohol (see *Discharge Instructions*).
- Treatment options for alcohol use disorder (see *Related Protocols*).
- The risks of combining alcohol with sedating substances.