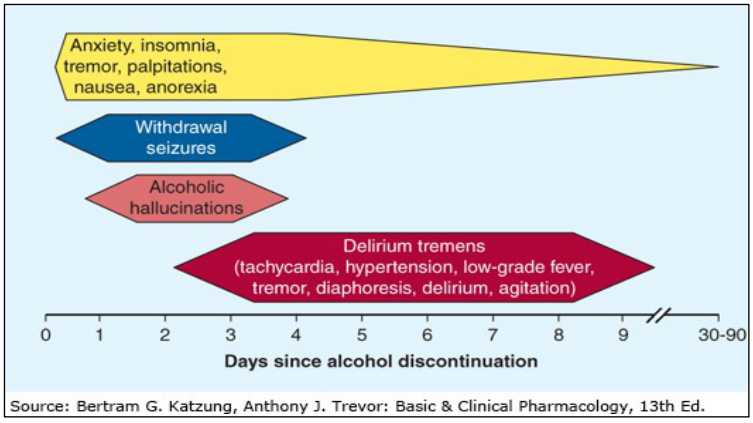
Clinical Pharmacology & Toxicology Pearl of the Week

~ Alcohol Withdrawal ~

Background

- ✓ Alcohol withdrawal (AW) is common and leads to increased morbidity and mortality.
- ✓ Chronic excessive alcohol intake causes central downregulation of inhibitory GABA receptors and upregulation of excitatory NMDA receptors to offset the depressant effects of alcohol.
- ✓ Abrupt cessation of alcohol leads to a state of imbalance between these inhibitory and excitatory neurotransmitters, which manifests clinically as the 4 stages of alcohol withdrawal (Figure 1).
- ✓ The LARS-10 and AUDIT-PC are used to predict a patient's likelihood of developing Severe Alcohol Withdrawal Syndrome (SAWS).
- ✓ The Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar) is commonly used to diagnose and assess the severity of AW.

Figure 1



Assessment and Management

- ✓ Assess for and investigate alternative and contributory diagnoses, including any underlying medical illness which may have caused the patient to stop drinking.

- ✓ For patients who have responded well to a single dose of benzodiazepines, continue treatment with symptom based triggered doses of diazePAM:
  - CIWA score of 10 to 19 = diazePAM 5 to 10 mg IV/PO every hour as needed.
  - CIWA score 20 or greater = diazePAM 10 to 20 mg IV every hour as needed.
  - If the CIWA score or clinical appearance does not continue to improve or worsens, increase diazePAM dose. Continue dosing frequency of every hour as needed.

- ✓ Patients with severe alcohol withdrawal (CIWA greater than 20) or who have significant agitation, autonomic instability, or delirium tremens require aggressive benzodiazepine administration in a closely monitored area to achieve rapid control of symptoms with frequent reassessments.
  - Administer diazePAM 10 mg IV (consider this Dose #1).
  - If the patient responds to Dose #1, continue with diazePAM 10 mg IV every 10 minutes as needed.
  - The goal is to achieve rapid sedation equivalent to a Richmond Agitation Sedation Scale of -1 to -2 (i.e., alert and calm to light sedation, briefly awaken to voice < 10 seconds).
  - If the patient does not respond to Dose #1, escalate the diazePAM dose following the dose escalation table below until clinical improvement is seen. The dose the patient responds to and causes clinical improvement will be considered the "effective dose."
  - Once the patient responds to a dose, stop escalating the dose and continue with the effective dose every 10 minutes as needed until control of symptoms and RASS -1 to -2.

- If the patient continues to have features of severe withdrawal despite escalating doses of diazePAM to 60 to 80 mg at a time, add PHENobarbital treatment following the directions below:
    - Continue to administer diazePAM every 10 minutes as needed.
    - Administer PHENobarbital 60 mg IV.
    - If severe symptoms persist after 30 minutes, administer PHENobarbital 120 mg IV push.
    - If severe symptoms persist after another 30 minutes, administer PHENobarbital 240 mg IV push.
    - Repeat doses of PHENobarbital 240 mg IV push every 30 minutes as needed until control of symptoms, to a **MAXIMUM DOSE** of 30 mg/kg.

✓ If the patient does not improve despite escalating doses of phenobarbital, or if at any point there is concern for the adequacy of the patient's airway or breathing, proceed with intubation and deep sedation (i.e., RASS -3 to -5) with propofol and midazolam infusions.

Additional pearls

✓ Medications such as gabapentin and clonidine may help control symptoms in mild but have not been shown to benefit severe withdrawal and should **NOT** be used as an alternative to benzodiazepines for an unwell patient.

✓ The onset and duration of benzodiazepines is highly variable. DiazePAM is the preferred benzodiazepine for alcohol withdrawal because it has a rapid onset of peak sedating effect, allowing frequent re-dosing with decreased risk of over sedation (dose stacking). The prolonged duration of effect additionally allows for "self-tapering" over several days as the patient's withdrawal gradually improves.

	Diazepam	Midazolam	Lorazepam
Peak effect (IV Route)	5 to 8 minutes	5 to 8 minutes	15 to 20 minutes
Onset of Sedation (IM Route)	Not recommended	5 to 10 minutes	20 to 30 minutes
Half-life	Active metabolites over 100 hours	2 to 4 hours	12 to 14 hours

✓ Patients with alcohol withdrawal are at increased risk for additional medical conditions as well as nutritional and electrolyte deficiencies. Therefore, assessment and treatment of concurrent conditions is important.

✓ Symptom triggered therapy results in shorter hospital stays, fewer complications, and lower likelihood of ICU admission when compared to fixed dosing of benzodiazepines.

The Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Calgary Zone Specialist Link. Click HERE for more details.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK).