



Clinical Pharmacology & Toxicology Pearl of the Week

~ Toxic Alcohols ~

Background

- A full review of toxic alcohol poisoning is beyond the scope of this Pearl. What follows are specific pearls and pitfalls in the diagnosis and management of toxic alcohol exposures.
- Figure 1 illustrates the metabolism of methanol and ethylene glycol.

Labs needed for most exposures

- Chemistry (Na⁺, K⁺, HCO₃⁻, Creatinine, Urea (BUN), Glucose)
- Serum osmolality
- Ethanol level
- Venous blood gas (VBG), if available
 - VBG is sufficient for most toxicologic exposures (unless the true pO₂ is important to know)
- **Note: very low risk exposures not referred to a health care facility do not need any outpatient testing and will be advised to watch for symptoms that warrant assessment by a health care provider.**

Labs needed for higher-risk exposures

- As above plus the following:
 - Urinalysis for calcium oxalate crystals
 - Note that crystals are not detected in about 1/3 of ethylene glycol exposures
 - Lactate
 - Methanol
 - Ethylene Glycol
 - Isopropyl alcohol and acetone
 - **Note: In PADIS's catchment area (AB, SK, NWT), testing for methanol, ethylene glycol, and isopropyl alcohol can only be performed in Calgary, Edmonton, Regina, and Saskatoon. Turnaround time is minimum of 3 hours from the time the lab receives the specimen**

Calculations

- Anion Gap (AG) = Na - (Cl + HCO₃)
- Calculated osmolality (SI units) = (Na x 2) + glucose + urea + (ethanol in mmol/L x 1.25)
 - "2 salts and some sugar in your bun"
- Osmol Gap (OG) = Measured osmolality - Calculated osmolality
- Both MD Calc and Micromedex have calculators for estimating blood concentrations of toxic alcohols and can be very helpful in determining need for specific treatment and/or transfer to a higher level of care

Treatment

Fomepizole

- Consider fomepizole if:
 - Ethylene glycol level greater than 3 mmol/L **OR**
 - Methanol greater than 6 mmol/L **OR**
 - Suspected ingestion + osmol gap greater than 10 **OR**
 - Suspected ingestion + serum pH less than 7.3 and serum bicarbonate less than 20 mmol/L
- Dose:
 - Loading dose IV: 15 mg/kg
 - Followed by 10 mg/kg every 12 hours for 4 doses
 - Then 15 mg/kg every 12 hours until:
 - Ethylene glycol or methanol levels are undetectable **OR**
 - Ethylene glycol level is below 3 mmol/L and the patient is asymptomatic with normal pH **OR**
 - Methanol level is below 6 mmol/L and the patient is asymptomatic with normal pH
- If patient dialyzed: change fomepizole dosing interval to Q4H during dialysis

Co-factors

- Methanol: folinic acid (leucovorin) or folic acid 50 mg IV Q4-6H until fomepizole and/or dialysis are discontinued
- Ethylene glycol: thiamine 100 mg IV once + pyridoxine 100 mg IV once + 2 g magnesium sulfate IV once (some resources suggest repeat dosing q6-8h for thiamine and pyridoxine)
- Correct metabolic acidosis (pH less than 7.2) with a sodium bicarbonate infusion (3 amps in 850 ml D5W with 40 meq KCl at 150 ml/hr)

Dialysis Indications

The EXTRIP website is an excellent resource for the most up to date recommendations on indications for extracorporeal removal in methanol and ethylene glycol poisoning (extrip-workgroup.org).

Repeat Labs

- If patient is staying in facility with no toxic alcohol testing available:
 - No fomepizole given → VBG, lytes, creat, glucose, and osmolality Q4H until medically cleared.
 - If fomepizole given → VBG, lytes, BUN, glucose, osmolality, and send out toxic alcohol level Q12-24H to determine need for further fomepizole dosing and when to stop treatment.
- If patient is staying in facility with toxic alcohol testing available:
 - Toxic alcohol level, VBG, and lytes Q12-24H to determine need for further fomepizole dosing and when to stop treatment.
- If dialysis performed → VBG, lytes, BUN, glucose, osmolality, and toxic alcohol level (if available) 2 hours before end of dialysis cycle to determine need for continued dialysis.

Tips/Pitfalls

- AG may be normal in early presentation; OG may be normal in late presentation
- The metabolic acidosis may take a minimum of 6 hours to appear in methanol poisoning, and 12 hours in ethylene glycol poisoning
- If no advanced testing (VBG, osmolality, toxic alcohols) available at the site, consider transfer of patient to higher level of care for investigations
- A normal osmol gap can be anywhere from -14 to +10, and what is abnormal depends on what the patient's normal gap usually is. The historical cutoff of a gap of +10 to prompt further workup may miss toxic alcohol exposures in those who normally have a low or negative osmol gap
- A “lactate gap” may be present in some ethylene glycol exposures where some of the toxic metabolites of ethylene glycol are falsely read as lactate by some blood gas analyzers. The gap is due to a difference between the blood gas lactate (falsely elevated) and the serum lactate on a chemistry analyzer (normal)
- An ethanol concentration greater than 22 mmol/L will completely inhibit alcohol dehydrogenase and may eliminate the need for urgent fomepizole dosing. Ethanol is eliminated at a rate of 3-4 mmol/hr in naïve drinkers, and 5-7 mmol/hr in chronic drinkers
- Isopropyl alcohol is metabolized to acetone (a ketone) and does not cause a metabolic acidosis unless there is another condition like GI bleeding, dehydration, or acute kidney injury
- There is no benefit to repeating toxic alcohol levels any more often than every 12-24 hours in patients who are not dialyzed. This is a labor-intensive test for the lab to run, and the kinetics of these alcohols are very long when fomepizole is used (methanol = 40-55 hours, ethylene glycol = 11-19 hours), making more frequent testing clinically unnecessary
- Not all patients with an elevated osmol gap and anion gap are toxic alcohol exposures. Causes for both elevated AG and OG (“the double gap”) include:
 - Methanol
 - Ketoacidotic states
 - diabetic, alcoholic, starvation
 - Lactic acidosis
 - Ethylene glycol/Diethylene glycol
 - Renal failure
 - Sepsis
 - Contrast dye

References

1. Ross et al. Toxic alcohol poisoning. Emerg Med Clin N Am. (2022).
2. Kraut et al. Toxic alcohols. N Engl J Med 2018; 378:270-80. DOI: 10.1056/NEJMra1615295

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm, excluding stat holidays. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral, Specialist Link, and RAAPID. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching “Pharmacology” from the ARD home page. Click [HERE](#) for more details about the service.

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). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching “Toxicology” from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

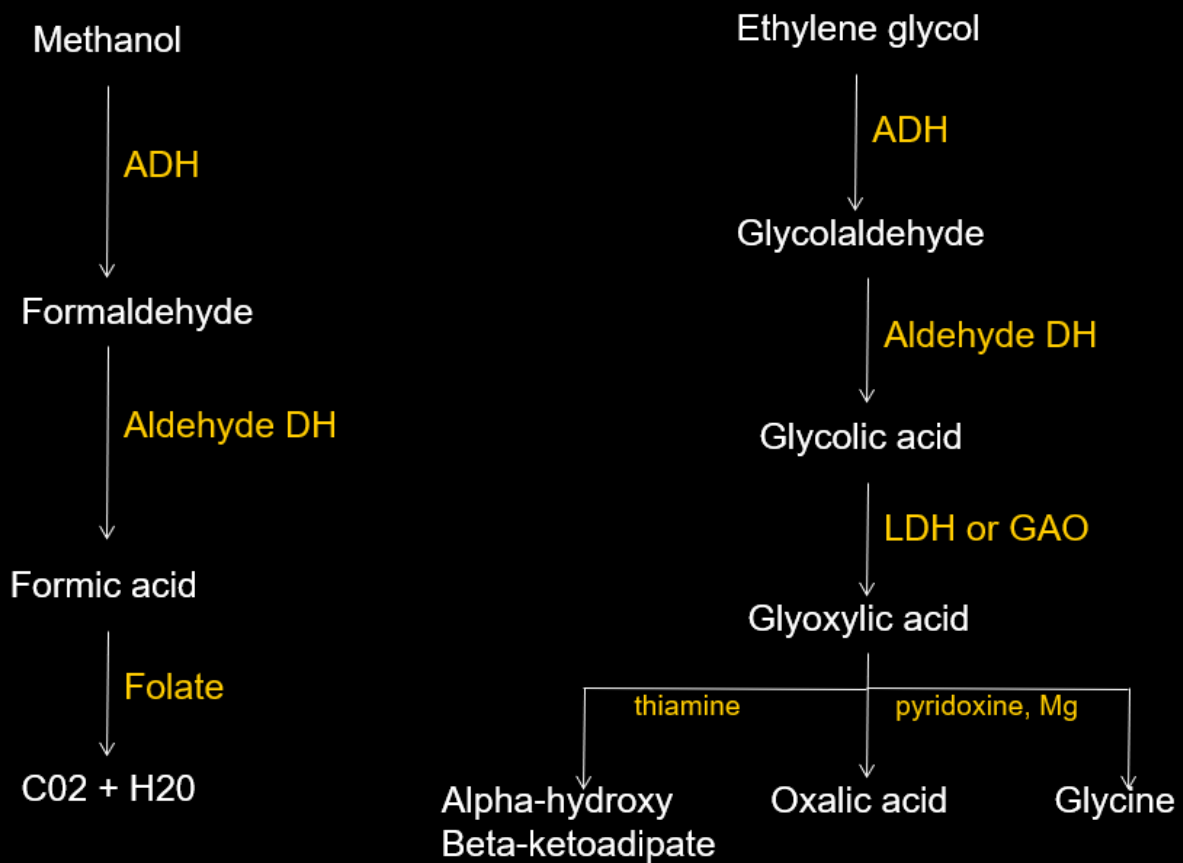


Figure 1. Metabolism of methanol and ethylene glycol, and the location of effect of the four cofactors (folate, thiamine, pyridoxine, magnesium). Fomepizole inhibits ADH, the first step in metabolism of both methanol and ethylene glycol.