EM CASES SUMMARY

# Episode 106 Toxic Alcohols – Minding the Gaps

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## Alcohols can be divided into two broad groups based on presentation, pathophysiology and management:

**The toxic alcohols are methanol and ethylene glycol,** which can both cause a scary anion gap metabolic acidosis in the first group and **ethanol and isopropyl alcohol** which aren't quite as scary and generally don't cause a big anion gap metabolic acidosis in the 2nd group.

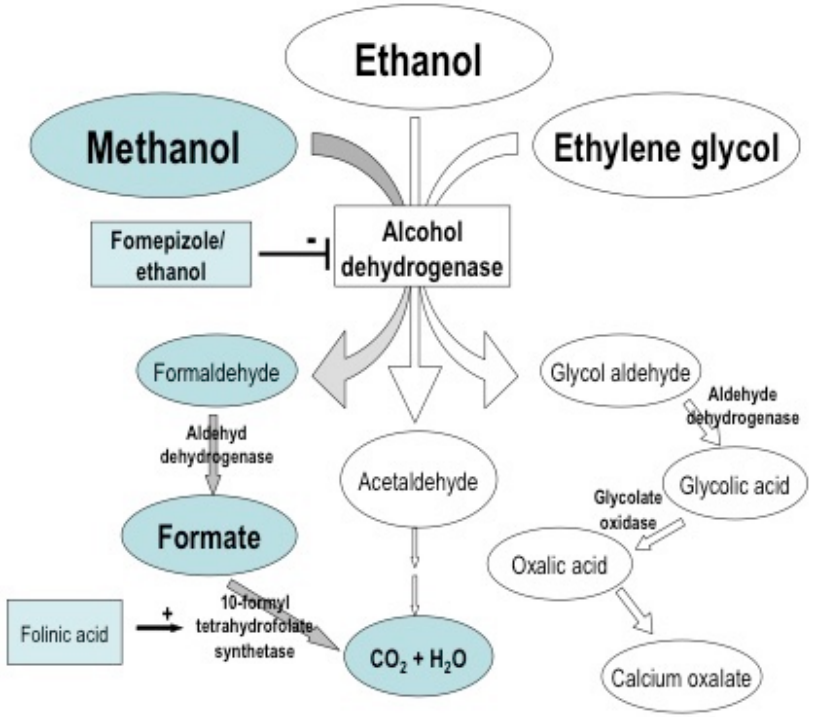
**Methanol** is commonly found in windshield-wiper fluid and de-icing products, as well as paint removers, shoe dyes embalming fluid, and surprisingly a number of Windex products.
**Ethylene glycol** is typically found in radiator antifreeze, degreasing agents, foam stabilizers and metal cleaners.

**Di-ethylene glycol** is also found in some anti-freeze products, and has caused outbreaks of renal failure after being inadvertently being substituted for sucrose.

**Isopropanol** is found in rubbing alcohol, hand sanitizer gels and other antiseptic preparations.

**Practical Pearl:** Call your local poison control center and request a product identification for products that you are unsure of the the contents.

Put simply, methanol and ethylene glycol get metabolized into acids which lead to optic neuritis (methanol) ATN/ARF (ethylene glycol) requiring specific treatments, while ethanol and isopropyl get metabolized into acetone which generally require supportive treatment only.



## Recognition of toxic alcohol poisoning: Clinical clues

While most toxic alcohol ingestions are recognized either on history or the finding of an anion gap metabolic acidosis, there are sometimes clinical clues that, if recognized, can lead to early initiation of time sensitive treatments. Early signs of both methanol and ethylene glycol toxicity are the same as for ethanol. When the alcohol is absorbed, before it is metabolized, these substances do cause GI upset (potentially nausea and vomiting), inebriation, slurred speech, nystagmus etc. As the alcohol is metabolized to an acid, hypotension develops, tachycardia, tachypnea, fixed dilated pupils for methanol, depressed level of awareness and potentially seizures.

### The 4 clinical clues to toxic alcohol poisoning are:

1. **Tachypnea** in absence of respiratory illness caused by patient's effort to blow off CO2 with their metabolic acidosis.
2. **Visual changes** with methanol include the classic *'snowstorm' vision*, blurry vision and ultimately blindness with fixed dilated pupils. The finding of extraocular movement paralysis with ethylene glycol is a very late finding and rarely seen in the ED.
3. **Not sobering up** as expected
4. **Seizure** may occur with severe toxic alcohol poisoning late in the presentation

## Recognition of toxic alcohol poisoning: Lab clues

Blood tests should not necessarily be ordered on every inebriated patient in the ED. For patients with any suspicion for a toxic alcohol ingestion, consider ordering a venous blood gas, calculated anion gap, osmolality, BUN, electrolytes and ethanol to calculate an osmolar gap, lactate, ketones and ASA level to sort out the anion gap metabolic acidosis and serum calcium.

### The 5 big lab clues to toxic alcohol poisoning are:

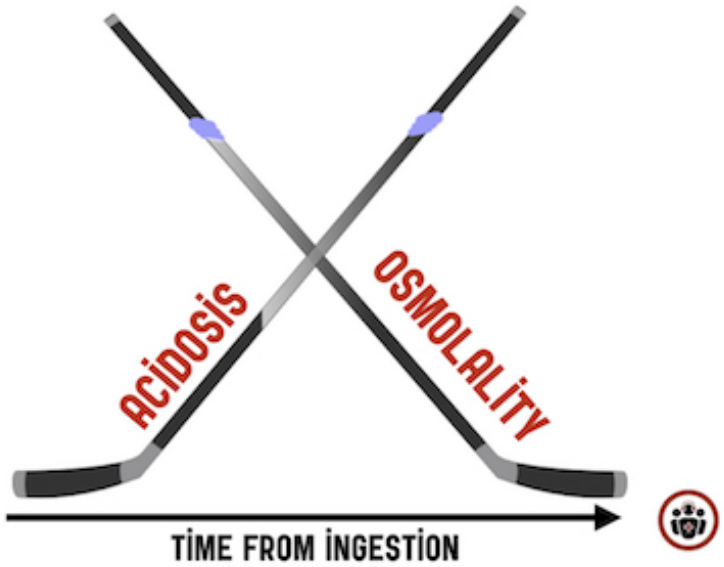
**1.AG metabolic acidosis.** Consider your GOLDMARK differential diagnosis of AG metabolic acidosis (download **PDF of GOLDMARK mnemonic**). Ethylene glycol may cause renal failure with an **elevated creatinine** contributing to the AG metabolic acidosis, while both methanol and ethylene glycol may cause an **elevated lactate**.
**Clinical Pearl:** The differential for a metabolic acidosis with a severely low bicarbonate level of 1 or 2 is small - severe sepsis, metformin induced and toxic alcohols

**2.High osmolality and osmolar gap.**
Osmolar gap calculation [2 x (Na)] + [glucose] + [urea] + [1.2 x ethanol]
In the United States: [2 x (Na)] +(glucose / 18) + (urea / 2.8) + (ethanol/4.1)

**Limitations of Osmolar Gap:** If a patient at baseline has a osmol gap of -14, and now has a osmol gap of 10, they have a elevated Osm Gap, even though it is considered normal by textbook definition. Sick patients from a variety of causes can have baseline osmol gap between +10 to +20. As the toxic alcohol is being metabolized to acid, the osmolarity decreases so that by the time you draw your blood work, the osmolar gap may be normal. High osmolar gaps are generally only seen *early* after toxic alcohol ingestion.

**Key concept:** The acidosis and osmolality in toxic alcohol poisoning are inversely related. As the patient becomes more acidotic the

osmolality decreases so that a normal osmolar gap does *not* rule out toxic alcohol poisoning. Think of their relationship like a pair of hockey sticks in a cross formation.




**3.Low ethanol level in an intoxicated patient.** While an ethanol level does not need to be drawn in every patient who presents to the ED inebriated, the serum ethanol may be a clue to a toxic alcohol ingestion. The patient with a decreased LOA with a negligible ethanol concentration must be investigated for other pathology. Ethanol is metabolized at the rate of ~ 5.5 mmol/L/hr in an induced patient. You can predict when the serum ethanol level should be low enough for that patient to mobilize safely out of the ED. If the patient is not improving in that estimated time, rethink the diagnosis and re-assess. For the toxic alcohol ingestion patient, who has co-ingested ethanol, the patient has treated themselves (for the time being), and does not need another intervention. Finally, the serum ethanol must be taken into account when calculating the osmolar gap.

**Pearl:** The triad of acidosis, high osmolality and low or zero ethanol level is highly suspicious for a toxic alcohol ingestion.

**4.Hypocalcemia with a prolonged QT** is sometimes seen with ethylene glycol toxicity as the calcium is bound to oxalate and deposits in the kidneys causing renal failure and in the brain causing the late findings of parkinsonism and basal ganglia hemorrhages.

**5.Bilateral basal ganglia hemorrhages** on CT (late finding) with ethylene glycol ingestion.

Note that urinary *calcium oxalate crystals* have very poor sensitivity and specificity for ethylene glycol toxicity and are therefore rarely helpful in the ED. In addition, wood's lamp examination of urine to detect fluorescein is rarely helpful in detecting ethylene glycol poisoning.

## Goals of management in toxic alcohol poisoning

1. **Block the toxic metabolites** with fomepizole or ethanol
2. **Correct pH** to 7.2 with bicarb
3. **Eliminate toxic metabolites** with dialysis (especially methanol)

## Time sensitive management actions in toxic alcohol poisoning

Note that there is a paucity of high level evidence for the following recommendations.

**Modify airway management for severe acidosis:** Consider delayed sequence intubation with ketamine if your patient is deemed an aspiration risk and *beware of the acidosis*; match the pre-intubation respiratory rate with post intubation respiratory rate and consider

bicarbonate boluses to avoid worsening acidosis and cardiovascular collapse.

**Call** your local poison control center +/- nephrology early.

**Prevent toxic metabolites:** Consider **fomepizole** ideally within 30 minutes. If you do not have access to fomepizole, consider **ethanol**.

**Fomepizole dosing:** loading dose of 15mg/kg, then 10mg/kg q12h for the first 48 hours, after which the dose is increased to 15mg/kg q12h
**Ethanol dosing:** oral ethanol q1h to a target serum ethanol level = 22-23 mmol/L. Note that if the patient comes in having co-ingested ethanol, they will not require fomepizole or additional ethanol as long as their serum ethanol remains above 22-23 mmol/L.

**Replenish cofactors:** Folic acid (50mg IV q4-6h) or folinic acid (1-2mg/kg IV q4-6h) for methanol; thiamine (100mg IV q6h) and pyridoxine (100mg IV q6h) for ethylene glycol.

**Correct acidosis** with a bicarbonate infusion to target pH = 7.2.
**Consider dialysis**: Dialysis may not be required if fomepizole is started early in ethylene glycol poisoning assuming there is no acidaemia or renal dysfunction. Methanol is eliminated too slowly for antidotal treatment alone to be effective and so usually requires dialysis.

Note that there is little, if any, role for GI decontamination in toxic alcohol ingestion because of rapid gastric absorption. NG suction may be considered within 30 minutes of ingestion.

**Pitfall:** A delay to dialysis in methanol poisoning is a common pitfall leading to poor outcomes. Call your nephrologist early!

## Indications for fomepizole or ethanol in toxic alcohol poisoning

1. Known ingestion of methanol, ethylene glycol or diethylene glycol without access to rapid serum osmolality
2. AG metabolic acidosis with elevated osmolar gap
3. Serum methanol >8 mmol/L
4. Serum ethylene glycol >3.2 mmol/L
5. Suspicion of toxic alcohol ingestion with evidence of end organ damage (ocular, renal)

## Indications for dialysis in toxic alcohol poisoning

1. Metabolic acidosis with evidence of end organ damage (ocular, renal, CNS)
2. Methanol >15 mmol/L
3. Ethylene glycol >6 mmol/L
4. Elevated osmolar gap if toxic alcohol levels not available

## Think of isopropyl alcohol poisoning as ethanol on steroids

Isopropyl alcohol, while technically is not a toxic alcohol, can cause morbidity and mortality and is more commonly ingested than the toxic alcohols. Isopropyl alcohol poisoning presents similarly to ethanol poisoning only more severely with coma and cerebellar signs, and it has more of a predilection for hemorrhagic gastritis and pancreatitis. Don't ignore abdominal complaints in patients with a history of alcohol misuse! Isopropyl alcohol is about twice as inebriating as is ethanol (for any particular load or blood level).

## Take home points for toxic alcohol poisoning

**Recognition: Clinical clues**

1. Tachypnea in absence of respiratory illness caused by patient's effort to blow off CO2 with metabolic acidosis
2. Visual changes
3. Not sobering up as expected
4. Seizure

**Recognition: Lab clues**

1. AG metabolic acidosis (caused by toxic alcohol +/- elevated lactate and renal failure)
2. High osmolality +/- osmolar gap (note that osmolality decreases with time)
3. Low ethanol level in intoxicated patient
4. Hypocalcemia with prolonged QT
5. Bilateral basal ganglia hemorrhages on CT (late finding)

**Goals of Management**

1. Block the toxic metabolites with fomepizole or ethanol
2. Correct pH to 7.2 with bicarb
3. Eliminate toxic metabolites with dialysis (esp methanol)

**Time sensitive management actions**

1. Airway – consider DSI with ketamine, match pre-intubation respiratory rate with post intubation respiratory rate and consider bicarbonate boluses to avoid worsening acidosis and cardiovascular collapse
2. Call poison control center +/- nephrology early
3. Consider fomepizole or ethanol to block toxic metabolites
4. Bicarbonate infusion to correct acidosis to pH = 7.2
5. Replenish cofactors
6. Consider dialysis in almost all methanol and some ethylene glycol poisoning

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