



The Blue Ridge Poison Center

# Tox Talks

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## Methanol and Ethylene Glycol Poisoning

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**THE UVA CENTER OF CLINICAL TOXICOLOGY** associated with the Blue Ridge Poison Center manages over 500 patients each year on site in the University of Virginia Health System - from outpatient clinic visits to critically ill inpatients managed in our pediatric and adult intensive care units. In addition, over 2,000 requests are made each year for consultation with our Boarded Medical Toxicologists from other healthcare facilities by phone or telemedicine. Call 1-800-222-1222 24 hours a day, every day. [Cell users: 1-800-451-1428]

### IN CHARLOTTESVILLE

Reminder: At University of Virginia Hospital, the first Wednesday of every month features toxicology Grand Rounds. For more information, contact Heather Collier: 434-924-5185 or [HLC8E@virginia.edu](mailto:HLC8E@virginia.edu)

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While all alcohols have some degree of toxicity, typically “toxic alcohol” is used to refer to ethylene glycol, methanol and in some cases isopropyl alcohol. Methanol and ethylene glycol poisoning result in an anion-gap metabolic acidosis, which is considered the hallmark of toxicity. Isopropyl alcohol is a gastric irritant and produces inebriation, but does not cause a high anion-gap metabolic acidosis. This discussion on toxic alcohols will focus on the diagnosis and management of methanol and ethylene glycol poisoning.

Methanol is a single carbon alcohol contained in many solvents, windshield washer fluid, gas additives, camping fuel and chaffing dish fuel. When ingested it may produce a mild amount of inebriation, but less so than an equivalent dose of ethanol. Methanol is metabolized sequentially by alcohol dehydrogenase and aldehyde dehydrogenase to the metabolites formaldehyde and formic acid, respectively. Formic acid is responsible for the anion-gap metabolic acidosis seen in methanol poisoning. The eyes and brain are particularly susceptible to methanol toxicity. Formic acid appears to be responsible for the majority of toxicity in both organs although the exact mechanism is unknown. Patients may complain of visual deficits on presentation. Papilledema along with retinal or optic disc pallor or hyperemia may be present on fundoscopic exam. Basal ganglia are the most commonly affected area of the brain; both ischemic and hemorrhagic lesions may be found on computed tomography scanning. The elimination half-life of methanol is long, typically from 30-54 hours; this may delay the onset of toxicity, but also may delay diagnosis, as the onset of acidosis may take many hours, while the toxic byproducts are slowly accumulating. Death may result from severe acidosis or central nervous system injury. Unfortunately visual deficits are often irreversible.

Ethylene glycol is a two carbon glycol that is most commonly found in antifreeze, but is occasionally used in other chemical and manufacturing processes. Its pure form is a sweet tasting compound making it attractive for children and animals. Ethylene glycol is metabolized by alcohol and aldehyde

dehydrogenase to acidic intermediates, with the end product being oxalic acid. Oxalate complexes with endogenous calcium forming calcium oxalate crystals. The primary organ of toxicity in ethylene glycol poisoning is the kidney, resulting from formation of calcium oxalate crystals with deposition in the renal tubules. In addition, there is some evidence that the acidic intermediates may be directly nephrotoxic. Deposition of calcium oxalate crystals occasionally occurs in other organs including the brain, spinal cord and heart leading to nervous system or cardiac dysfunction. Death may occur from severe acidosis, renal failure, or occasionally direct cardiac or central nervous system injury. Renal failure is often reversible but may require long term dialysis.

Diagnosis of toxic alcohol poisoning consists of a thorough history, along with physical exam and recognition of laboratory abnormalities associated with poisoning. Patients may or may not appear inebriated based on the amount of toxic alcohol consumed. While “classic” laboratory criteria for methanol and ethylene glycol poisoning include anion-gap metabolic acidosis with an osmol gap, this is not always the case. Early in the course of intoxication when the parent compound is yet to be metabolized, an osmol gap may be present without a concurrent anion gap. Conversely, late in the course of presentation when the parent compound has been fully metabolized, the osmol gap may be normal while a large anion-gap metabolic acidosis will be present. It is important to note that the osmol gap can be used as a screening test, but should never be used to confirm or disprove a diagnosis of toxic alcohol poisoning. Variations occur in normal human serum osmolality so that interindividual ranges in osmol gap may be from approximately -10 to +10. This means that low or normal osmol gaps may “hide” a significantly high level of methanol or ethylene glycol. Methanol and ethylene glycol levels are helpful in confirming diagnosis, but are often not readily available as measurements are made by gas chromatography/mass spectroscopy. Hypocalcemia may be found in ethylene glycol poisoning secondary to chelation of calcium. An elevated creatinine is a marker of renal injury. Contrary to customary belief, urine fluorescence is neither a sensitive nor specific indicator of ethylene glycol poisoning.

Ethanol competitively inhibits the metabolism of both methanol and ethylene glycol by alcohol dehydrogenase, blocking production of their acidic metabolites. Intravenous ethanol is an inexpensive antidote, however is difficult to maintain at a therapeutic level, and produces inebriation along with occasional hypoglycemia, necessitating a higher degree of nursing care, close monitoring and frequent ethanol and glucose checks. This may lead to higher hospital costs in the long run. An initial intravenous dose of 8-10cc/kg followed by 1-2 cc/kg/hr of a 10% ethanol solution will typically achieve the 100mg/dL blood ethanol level needed to block the metabolism of ethylene glycol or methanol. While infusing ethanol, a blood ethanol level and blood glucose should be checked every 1-2 hours.

Fomepizole (4-methylpyrazole) is a competitive alcohol dehydrogenase inhibitor that has a higher per dose cost than ethanol, but is dosed IV every 12 hours, does not produce inebriation or other laboratory abnormalities and in uncomplicated patients (most unintentional pediatric or adult cases) does not necessitate the higher level of nursing care that ethanol infusion does. Initial loading dose is 15 mg/kg, followed by 10 mg/kg every 12 hours for 4 doses if the patient is not on dialysis. If additional dosing is needed the 15 mg/kg dose is used, as fomepizole, like ethanol, induces its own metabolism. Generally, fomepizole or ethanol infusion should be administered for a methanol or ethylene glycol level greater than 20 mg/dL, or clinical suspicion of poisoning along with metabolic acidosis or an osmol gap. Keep in mind that neither ethanol or fomepizole will affect the already formed metabolites, these agents only block further formation of acidic metabolites.

Hemodialysis is the definitive treatment for methanol and ethylene glycol poisoning, effectively removing both the parent compound and the organic acid metabolites. General recommendations for initiation of dialysis include presence of severe acidosis, a methanol or ethylene glycol blood level greater than 50 mg/dL, renal failure, neurologic dysfunction (other than inebriation) or visual impairment. As both ethanol and fomepizole are dialyzable their dosage rates will need to be adjusted during dialysis.

Methanol and ethylene glycol poisoning should be in the differential diagnosis of all patients presenting with an anion-gap metabolic acidosis. These agents produce toxicity through metabolism to toxic byproducts. Management centers on blocking metabolism of the parent compound through administration of ethanol or fomepizole, and initiation of hemodialysis in the appropriate clinical context.

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