Commentary

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This case of a patient with ethylene glycol poisoning illustrates the difficulty of diagnosing the ingestion of this toxic alcohol. Traditionally, such poisoning is recognized by ethylene glycol's tendency to cause an increase in the serum osmolal gap with and without an increase in the serum anion gap. The increase in the osmolal gap is due to accumulation of the parent alcohol, whereas the increase in the serum anion gap is due to accumulation of the organic-acid metabolites. Therefore, early on in the course of poisoning (before extensive metabolism of the alcohol), only an increase in the osmolal gap might be observed. Subsequently, increased osmolal and anion gaps can be observed as the alcohol is metabolized. Finally, when the bulk of the alcohol has been metabolized, only an increased anion gap might be seen.

Additional factors that can affect the pattern of the osmolal and anion gaps include their baseline values. The authors correctly identify that the baseline osmolal gap in an individual can be low. Individuals with a very low gap might have a large concentration of the alcohol without the osmolal gap increasing above the upper reference limit. One issue not addressed by the authors was the possibility that the 18-mmol/L anion gap at presentation might be increased although remaining within the normal range. The reference range of the anion gap is wide, spanning 10 mmol/L from low to high *(1)*. Therefore, an individual with a value at the low range of normal could have a large accumulation of organic acids without a detectable increase in the anion gap.

Be that as it may, the authors correctly identify the difficulty of diagnosing a toxic-alcohol exposure, the need for early use of an analytically sensitive test to detect its presence, and the importance of having a high level of suspicion for toxic-alcohol exposure for all patients.

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Reference

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Commentary

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One of the best-known mnemonics in medicine is MUDPILES (for methanol, uremia, diabetic ketoacidosis, propylene glycol, isoniazid, lactic acidosis, ethylene glycol, salicylates), which helps us remember causes of increased anion gap metabolic acidosis. Less well known is ME DIE (for methanol, ethanol, diuretics such as mannitol, isopropyl alcohol, ethylene glycol), which helps us remember causes of increased osmolal gaps.

Ethylene glycol appears in both mnemonics; the only other compound with that distinction is methanol. Both are central nervous system depressants in their unmetabolized forms, but their major toxicities occur when they are converted into their strong-acid metabolites. By blocking their metabolism, one prevents their most dire consequences.

Because most clinical laboratories must refer samples elsewhere for measurement of ethylene glycol, and probably methanol, and because delays can only exacerbate their toxicities, treatment, appropriately, is often presumptive. If the concentrations of these alcohols are low, treatment can be discontinued.

While awaiting definitive measurements of these alcohols, clinicians may turn to surrogate tests, such as

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the anion gap or the osmolal gap. Strong acids produced by metabolism of ethylene glycol and methanol are present in appreciable millimolar concentrations and are detectable as an increased anion gap. Unfortunately, that is not the case for both parent compounds, whose presence is reflected in the osmolal gap, rather than anion gap. Because of their respective molecular weights (32 and 62 mg/mmol) and lethal concentrations (80 and 20 mg/dL), methanol at its lethal concentration will create a sizable osmolal gap (25 mOsm/kg), whereas ethylene glycol will not (3 mOsm/kg).

As reflected in this case, treatment for possible ethylene glycol ingestion should be presumptive to prevent acidosis. A normal osmolal gap should not be used to rule out toxic concentrations, initially or during treatment; genuine ethylene glycol concentrations are needed. Clinical chemists occupy a strategic position to ensure treatment is not delayed while awaiting results and to caution against the use of insensitive surrogate tests.

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