What’s Trending: A Case of Type B Lactic Acidosis Due to Propylene Glycol Exposure
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**BACKGROUND**
The finding of lactic acidosis is concerning in any critically ill patient, as it is potentially a sign of inadequate oxygenation of tissues, leading to excess production of lactic acid. As illustrated below, lactate is produced in anaerobic environments preventing the continued metabolism of pyruvate through the glycolytic cycle within the mitochondria:

However, there are many reasons outside of anaerobic metabolism, referred to as type A lactic acidosis, which can cause the accumulation of lactic acid, which are collectively referred to as type B lactic acidosis. The etiologies of the latter are attributable to a decrease oxygen utilization, excess non-hypoxia related lactate generation, and decreased lactate clearance. The underlying causes include diabetes, malignancy, the use of total parenteral nutrition, HIV, and a large variety of prescription drugs and toxins alike. Differentiation between the two types of lactic acidosis, especially in critically ill patients, can be very difficult.

**THE CASE**
A 50 year old man with a past medical history significant for multiple psychiatric diagnoses and prior admissions for suicidal ideation, type II diabetes on metformin, and alcohol abuse with a history of alcohol withdrawal seizures, was admitted to the medical ICU after an intentional ingestion of trazodone and alcohol. He was intubated en route to the hospital for airway protection, and started on alcohol withdrawal protocol. Vitals were notable for the patient being afebrile, tachycardic, slightly hypertensive, with normal oxygen saturation. Initial laboratory evaluation was revealing for:

- ABG: 7.25/47/249/20
- Lactic acid trend (mmol/L): 8.26 —5 hours—> 146 107 10 160
- Anion Gap: 18
- Tylenol and salicylate levels: undetectable
- Ethanol (serum): 355

Lactic acid trend (mmol/L):
4.9 —4 hours—> 5.2 —5 hours—> 5.1

His persistently elevated lactate at this time, in the absence of any evidence of tissue hypoperfusion, was attributed to a variety of type B causes, including acute alcohol intoxication, type II DM, and delayed clearance through the liver. However in the spirit of being cautious, a repeat lactate level was ordered for the next morning.

**THE CASE, CONTINUED**
The next morning after admission, routine laboratory testing revealed a persistently elevated lactate at 5.7, and additionally:

- Osmolar gap: 34 (abnormal: > 10)

The patient remained hemodynamically stable, but concern grew on rounds as a repeat lactate was again elevated at 7.9. An urgent abdominal exam was performed which was unrevealing, however the patient was then taken for an abdominal CT, which was unrevealing for bowel ischemia.

The differential for type B lactic acidosis, specifically with an elevated osmolar gap, was reviewed, and it was noted that the patient’s alcohol withdrawal protocol called for very large doses of benzodiazepines. This patient received a total of 1,920 mg of IV diazepam in the last 24 hours, which contains propylene glycol as the carrier solvent. The doses received are pictured:

After discontinuation of the diazepam, a follow up lactate 5 hours later was 2.9, the next morning was 1.1, and there was complete resolution of the gap acidosis.

**DISCUSSION**
This case adds to published case reports of lactic acidosis with an elevated osmolar gap due to propylene glycol exposure. About 55% of propylene glycol is metabolized to lactate. This patient did not have acute kidney injury which had also been described.

The finding of an elevated lactate is very concerning. Prospective studies of critically ill patients have found decreased survival with lactate levels > 3.5 mmol/L. Thus, the urgent search for the etiology of this patient’s elevated lactate was warranted. However, looking back, a more thorough examination of the differential for a likely type B lactic acidosis, as type A seemed very unlikely, would have been prudent, and perhaps would have avoided an urgent CT. Some agents causing type B lactic acidosis:

**Table 3. Drugs and Toxins**

<table>
<thead>
<tr>
<th>Biguanides</th>
<th>Antiretroviral drugs</th>
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<tbody>
<tr>
<td>Ethanol</td>
<td>Propylene glycol</td>
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<tr>
<td>Propofol</td>
<td>Vasovactive drugs</td>
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<td>β-2 Agonists</td>
<td>Theophylline</td>
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<td>Salicylate</td>
<td>Isoniazid</td>
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<tr>
<td>Nicin</td>
<td>Nalidix acid</td>
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<td>Simvastatin</td>
<td>Acetaminophen</td>
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<td>Cyanide</td>
<td>Nitroprusside</td>
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<td>Lactulose</td>
<td>Lineozolid</td>
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Hopefully we all can learn from this case, and recognize propylene glycol as a cause of lactic acidosis, in the future.

**References:**