CASE PRESENTATION
A 48-year-old male with history of depression admitted to the intensive care unit (ICU) after ingesting >500 tablets of extra-strength Asptomphen. N-Acetylcysteine infusion was initiated and patient mechanically ventilated due to impending respiratory failure.

Physical Exam:
- Intubated, sedated
- Allevia, HR 94, BP 135/65, RR 20, Pox 95% on 40% FiO2
- Cardiac: normal
- Abdominal, Rectal: normal
- Lab:
  - Acetaminophen level: 800 mg/L
  - Lactic Acid: 10.8 mmol/L
  - Serum Osmolality: 295 mOsm/kg
  - Acetaminophen: 0 mOsm/kg
- Anion Gap: 16 mmol/L

On day 1, patient was maintained on NAC infusion. He required volume resuscitation and initiation of vasoressor infusions to maintain effective circulation. Over the next several hours, lactate level decreased and yet patient developed worsening anion gap metabolic acidosis. Other usual culprits for presence of anion gap (sialylate, ketones, uremia) were absent. He had to be deeply sedated and transiently paralyzed to promote patient-ventilator synchrony. Even though he had no osmolar gap, illicit alcohol screen was checked and was positive for methanol. Patient was initiated on fomepizole and CRRT.

HOSPITAL COURSE
- Day 1: NAC infusion, unexplained worsening AGBWA with normal osmolar gap, surmising positive for methanol
- Day 2: CRRT continued
- Day 3: worsening liver injury, cerebral edema
- Day 4: hypothermia protocol
- Day 5: Upper GI bleed, EGD, suggestive of caustic ingestion
- Day 6: Central edema improved, rewarming process
- Day 7: stable hemodynamics
- Day 11: Extubated
- Day 12: normal mental status, normal MRI brain; Psychiatry evaluation
- Day 13: Transfer to medical floor
- Day 18: Discharged from the hospital

OBJECTIVES
- Define osmolal gap
- Discuss causes of high osmolal gap
- Normal osmolal gap does not rule out methanol toxicity

DISCUSSION:
Chemistry:
- Methanol: an alcohol which is sequentially metabolized by alcohol dehydrogenase to formic acid and then formic acid. Osmolar gap is caused by presence of alcohol, as it is an unmeasured osmole. Toxicity however is caused by formic acid, which exists at physiologic pH as formate. Formate causes anion gap.
- Early in the toxicity, patients have osmolar gap; however when presenting late, most of methanol is now metabolized to formate; and they may have no osmolar gap, only unexplained anion gap.

PATHOLOGY FINDINGS:
- Latent period corresponds to conversion of methanol to formate
- Symptoms develop 12-24 hours after ingestion
- Kussmaul respirations, weakness, headache, nausea, severe epigastric pain, visual disturbances, blindness
- Memory loss, confusion, agitation
- Stupor, coma

LABORATORY FINDINGS:
- Elevated Anion Gap Metabolic Acidosis
- Increased formic acid (this is not routinely measured)
- Elevated Osmolar Gap
- Elevated lactic acid
- Positive serum methanol assay

TAKE HOME POINTS
- The gold standard for diagnosing methanol toxicity is gas chromatography.
- Results can take up to days and many hospitals are not equipped to provide this test.
- Clinicians must rely on the clinical presentation and other laboratory tests such as osmolar gap (OG) to make a diagnosis.
- Normal osmolar gap does not rule out methanol toxicity.
- If suspicion of methanol toxicity is high, treatment with fomepizole or ethanol should be initiated promptly pending methanol levels.
- Other times, toxisomes and ingestions co-exist. Thus high index of suspicion is warranted in unexplained anion gap metabolic acidosis.

TREATMENT OF METHANOL POISONING
- Endotracheal intubation, supportive care
- Administration of ethanol or fomepizole (blocks Alcohol Dehydrogenase)
- Initiation of renal replacement therapy

REFERENCES