A 31-year-old previously healthy man presented with a 7-day history of nausea, intractable vomiting, diffuse abdominal pain, and progressive blurred and tunnel vision.

**Physical Examination**

Vital signs: temperature, 37.1°C; pulse, 85 beats/min; respirations, 32/min; BP, 155/93 mm Hg. General alert, oriented. Eyes: no light perception, pupils 8 mm bilaterally and unresponsive to light, mild edema of the right optic disk. Chest, cardiac, and abdominal examinations: unremarkable.

**Laboratory Findings**

Na⁺, 139 mmol/L; K⁺, 2.8 mmol/L; Cl⁻, 110 mmol/L; HCO₃⁻, 7 mmol/L; BUN, 17 mg/dl; glucose, 130 mg/dl. Serum acetone, 0 mg/dl; lactate, 1.8 mmol/L; salicylate, 1.2 mg/dl; osmolality, 306 mosm/L. Arterial blood gas values (room air): pH, 7.24; Pco₂, 17 mm Hg; Po₂, 128 mm Hg. Urinalysis: 0 to 2 WBC, 0 to 2 RBC, no crystals, negative ketones.

**What laboratory tests should be ordered next? What is the therapy for the suspected diagnoses?**

**Answer:** Serum ethylene glycol and methanol levels should be ordered next. Intravenous infusion of HCO₃⁻, ethanol, and folate and hemodialysis should be instituted.

The differential diagnosis of an elevated anion gap in the setting of an osmolar gap greater than 10 mosm/L suggests the clinical diagnosis of ethylene glycol or methanol intoxication. The presence of visual disturbances increases the probability of methanol poisoning because of the high incidence of retinal damage.

Methanol is an odorless and colorless alcohol that is derived from the distillation of wood. Methanol is an important component of various paints, varnishes, antifreeze solutions, plastics, inks, and dyes, and its ingestion produces a drunken state similar to that which follows drinking of ethanol. In contrast to ethanol, however, metabolic oxidation of methanol by alcohol dehydrogenase produces toxic levels of formaldehyde and formic acid. The lethal dose of methanol varies greatly among individual patients and depends on several clinical factors. For instance, the concurrent ingestion of ethanol may be protective because of saturation of alcohol dehydrogenase, which prevents the formation of toxic methanol metabolites. In contrast, folate deficiency may enhance methanol toxicity, since the metabolic elimination of formate through formation of carbon dioxide appears to be folate-dependent.

Toxic clinical manifestations of methanol ingestion begin after a 10- to 20-h latent period. Common symptoms include headache, nausea, vomiting, abdominal pain, progressive confusion, and visual abnormalities that can progress to blindness. Physical signs include dilated and nonreactive pupils, with hyperviscosity and edema of the optic disks.

In the absence of a clear-cut ingestion history, laboratory abnormalities present the most important clue to diagnosis. Methanol is a low-molecular-weight substance that produces an anion-gap metabolic acidosis and increases measured serum osmolality. If the measured osmolality is 10 mosm greater than the calculated osmolality (Posm = 2[Na⁺] + glucose/18 + BUN/2.8) and the measured osmolality is high (>295 mosm/L), methanol intoxication can be presumed. Although an osmolar gap can also occur after ingestion of isopropyl alcohol or ethylene glycol, only methanol is associated with the combination of characteristic visual disturbances and metabolic acidosis.

These clinical findings warrant a prompt serum assay for methanol.

When clinically suspected, therapy should be initiated even before confirmation of the diagnosis by blood test analysis. Goals of therapy include correction of systemic acidosis, prevention of further metabolism of methanol to formate, and the rapid elimination of toxic levels of methanol and formate from the blood.

Correction of profound metabolic acidosis requires...
intravenous infusion of bicarbonate or hemodialysis in the setting of intractable acidemia or renal failure. Prevention of further methanol metabolism is achieved by the intravenous infusion of ethanol, which has a higher affinity for alcohol dehydrogenase. A loading dose of 0.6 g/kg of 10 percent ethanol is given, followed by a maintenance infusion of 66 mg/kg/h in non-drinkers or 150 mg/kg/h in drinkers. The goal of therapy is to maintain a blood alcohol level of 100 mg/dl until all measureable serum methanol has been eliminated. Some experts recommend continuing the ethanol drip for an additional 48 h because of a possible rebound phenomenon.

Rapid elimination of methanol and formate from the blood requires hemodialysis. Indications include metabolic acidosis unresponsive to intravenous bicarbonate, the presence of any visual disturbances, and a serum methanol level greater than 50 mg/dl. To maintain adequate serum ethanol levels during hemodialysis, ethanol infusions usually require upward adjustment. Most experts recommend continuing hemodialysis until methanol levels decrease below 20 mg/dl. Adjunctive therapy includes intravenous administration of folate (50 mg every 4 h) because the oxidative conversion of formic acid to carbon dioxide appears to be folate-dependent.

Patient prognosis is most dependent on the severity and duration of metabolic acidosis after methanol ingestion. Patients who are admitted to the hospital more than 24 h after ingestion have the worst outcome. Permanent visual disturbances correlate not only with the severity of acidosis, but also with the initial visual limitation, the degree of loss of pupillary reflex, and the presence of profound edema of the retina. Approximately 15 percent of patients who present with visual impairment are left with permanent sequelae.

The present patient had visual disturbances and an osmolal gap that suggested methanol intoxication. Therapy was initiated with intravenous bicarbonate, ethanol, and folate combined with a 6-h course of hemodialysis. The admission serum methanol level subsequently was reported at 37 mg/dl and decreased to 10 mg/dl the following day. Despite rapid correction of acidosis and elimination of methanol, the patient did not regain his sight, remaining permanently blind.

**Clinical Pearls**

1. Methanol intoxication should be suspected in a patient with nausea, vomiting, abdominal pain, visual changes, and a combined anion and osmolal gap.

2. Intoxication from methanol can occur via ingestion, inhalation, or skin absorption.

3. Immediate treatment to correct the acidosis with bicarbonate, intravenous ethanol, and, in some cases, hemodialysis should be initiated as soon as the diagnosis is suspected to improve prognosis.

4. Intravenous folate may accelerate the oxidative elimination of formate generated from the metabolism of methanol.

**Suggested Reading**


