

# Don't Always Rush to Rally Renal

Anita Mudan, MD; Lewis S. Nelson, MD

A 20-month-old boy presented for evaluation after ingesting a model race car fuel additive.

## Case

An otherwise healthy 20-month-old boy presented to the ED for evaluation after his father witnessed the child ingest a model race car fuel additive. According to the patient's father, the boy was playing with several closed bottles that were stored in the garage, when he witnessed the boy open up and take a sip of a pink-colored fuel additive, which the father believed to contain 100% methanol. The patient's father further noted that immediately after drinking the fluid, the patient spat and drooled, and had one episode of nonbloody emesis prior to arrival at the ED.

Initial vital signs at presentation were: blood pressure, 84/54 mm Hg; heart rate, 97 beats/min; respiratory rate, 24 breaths/min; and temperature 98°F. Oxygen saturation was 99% on room air. Physical examination was notable for mild erythema in the posterior oropharynx. Otherwise, the patient was acting appropriately for his age and in no acute distress. Laboratory studies were within normal limits, except for the following: serum anion gap, 18 mEq/L (reference range for children <3 years old, 10-14 mEq/L); serum bicarbonate, 19 mmol/L (reference range for children 12-

24 months, 17-25 mmol/L); and serum creatinine, 2.8 mg/dL (reference range for children 12 to 24 months, 0.2-0.5 mg/dL). A repeat creatinine test taken after bolus of fluid administration was 2.4 mg/dL. A renal ultrasound, performed to investigate the cause of the renal failure, was unremarkable.

## What toxic exposures are of concern based on the clinical history?

The history of exposure to a liquid stored in a garage raises the likelihood of exposure to an automobile-related item such as diethylene glycol, ethylene glycol (EG), and methanol.

**Diethylene Glycol.** Diethylene glycol is an ingredient in brake and power steering fluids, and has toxic properties qualitatively similar to EG.

**Ethylene Glycol.** A clear, colorless, odorless fluid with a sweet taste, EG is an ingredient in radiator antifreeze, refrigerant fluid, coolants, and pesticides. Like methylene, EG reaches peak plasma concentration within 1 to 4 hours, but toxic clinical findings do not occur for 3 to 6 hours.<sup>1</sup>

**Methanol.** Methanol is a clear, colorless, alcohol found in antifreeze, windshield

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**Dr Mudan** is an emergency medicine resident, department of emergency medicine, University of Pennsylvania, Philadelphia. **Dr Nelson**, editor of "Case Studies in Toxicology," is professor and chair of the department of emergency medicine, Rutgers New Jersey Medical School; and a medical toxicologist, New Jersey Poison Information & Education System, both in Newark. He is also associate editor, toxicology, of the EMERGENCY MEDICINE editorial board.

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washer fluid, and race car fuel.<sup>2</sup> Although methanol reaches peak plasma concentration in about 30 to 60 minutes, signs of systemic toxicity (ie, metabolic acidosis) typically take 6 to 12 hours to manifest.<sup>1</sup>

In both EG and methanol, there is a delay in toxic clinical findings because the parent compounds are not toxic in their initial form; rather, major toxicity is derived from their metabolites: formic acid and oxalic acid, respectively.

**Other Toxins.** Many other potentially toxic liquids are associated with a homeowner's occupation or avocational interests. These include painting supplies (eg, industrial paints containing lead), gardening materials (eg, pesticides containing organophosphates), fuels (eg, gasoline, polychlorinated biphenyls in coolant, and lubricants), and cleaning supplies (eg, caustics, detergents, and air freshener).

### Case Continuation

Since the patient's elevated anion gap raised concerns for methanol or EG exposure, he was given fomepizole and transferred to a tertiary care children's hospital for further management and possible hemodialysis. Upon arrival at the receiving hospital, the patient's vital signs and physical examination remained unchanged. Repeat laboratory studies were notable for a creatinine level of 0.3 mg/dL. The patient's father was instructed to retrieve the implicated bottle from home. An inspection of the bottle's ingredients was notable for nitromethane, castor oil, and methanol.

### What is nitromethane and what are its uses?

Nitromethane, the simplest nitro compound, is a colorless, viscous, lipid-soluble fluid.<sup>3</sup> The polarity of nitromethane permits its use as a stabilizer in a number of chemical solvents, such as dry cleaning fluid, degreasers, and "super glue."<sup>4,5</sup> Nitromethane is also commonly added to model-engine and drag-race fuels, which also contain methanol and castor oil.<sup>3</sup> In this capacity, nitromethane functions as



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an oxygen carrier, allowing more efficient fuel use in combustion cylinders (compared to gasoline), thereby increasing the horsepower of the vehicle.<sup>6</sup> It is therefore commonly added to fuel for drag racers, radio-controlled cars, and model aircrafts.<sup>4</sup> In the small concentrations typically inadvertently ingested, the clinical effects of nitromethane itself are inconsequential.

### What is the differential for creatinine elevation?

Creatinine itself is a normal breakdown product of muscle metabolism produced by spontaneous conversion from creatine and is found at a fairly constant serum level in proportion to muscle mass.<sup>7</sup> Thus, as people age and muscle mass decreases, their baseline creatinine levels decrease proportionally.

**Elimination.** The majority of creatinine (85%-90%) is filtered and excreted by the kidneys, with the remaining 10% to 15% secreted by the tubules, allowing creatinine to be a surrogate measure of the glomerular filtration rate.<sup>7</sup> Exogenous sources of creatine or creatinine include meat and creatine supplements, the latter of which are used as an "energy source" to enhance athletic performance.

**Etiology.** The etiology for an elevated serum creatinine concentration includes

renal failure, both acute and chronic; volume depletion; hemorrhage (low blood volume); and medications, including diuretics, angiotensin converting enzyme inhibitors, angiotensin-receptor blockers, nonsteroidal anti-inflammatory drugs, and certain antibiotics. These etiologies can also be categorized as processes that increase creatinine production, decrease elimination ( $H_2$  antagonist and trimethoprim both inhibit the cation secretory pump in the tubules), or interfere with the creatinine assay (ketones, keto acids, lipemia, hemolysis, cephalosporins).<sup>7</sup>

Because creatinine is filtered so efficiently by the kidney, neither exogenous nor endogenous creatinine sources are expected to increase serum creatinine in the absence of renal dysfunction. However, transient elevation may occur in body builders who use extreme doses of creatine. Patients with rhabdomyolysis often develop elevated creatinine concentrations, but nearly always in the setting of myoglobinuric renal failure.

**Jaffe Reaction and Enzymatic Methods.** Serum creatinine can be measured using either the Jaffe reaction or the enzymatic method. In the Jaffe reaction, creatinine reacts with alkaline sodium picrate to form a red-orange chromophore, which absorbs light in the range of 470 to 550 nanometers on spectroscopy.<sup>6,8,9</sup> The active methylene group on nitromethane also reacts with alkaline sodium picrate to form a chromophore which absorbs light in the same wavelength range.<sup>10</sup> Thus, serum creatinine measurements via the Jaffe reaction are falsely elevated due to the cross-reactivity between nitromethane and alkaline sodium picrate. In some reported cases, there is a 20-fold increase in the measured serum creatinine in the presence of nitromethane; renal function, however, remains normal.<sup>5</sup>

This false reading seen in the Jaffe reaction can be avoided by utilizing the enzymatic method of creatinine measurement, a three-step process that ultimately pro-

duces hydrogen peroxide, which is measured and accurately correlates with serum creatinine—even in the presence of nitromethane.<sup>8</sup> This distinction explains the dramatically different creatinine concentrations measured at the two institutions in this case.

### Case Conclusion

The patient was monitored overnight at the children's hospital. Repeat laboratory studies in the morning showed a normal creatinine level of 0.3 mg/dL and a negative methanol level. The patient was discharged home in the care of his father, who was instructed to follow-up with his son's pediatrician. The father also received counseling on safe storage practices for dangerous chemicals.

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