Central New York Regional Poison Control Center

The CNYPCC

# Toxicology Letter

October, 2001

Vol. VI No. 4

A Quarterly Publication

## SCHEDULED EVENTS:

Emergency Medicine Grand Rounds
Health Sciences Library Room 318
Second Wednesday of the Month, 11:00 AM

Toxicology Case Conference
CNYPCC, 550 E Genesee Street
Poison Center Conference Room
Every Thursday 1:30 PM – 2:30 PM

## PROGRAM ANNOUNCEMENT:

Please watch for our brochure for the Fifth Annual Toxicology Teaching Day on November 7, 2001 at the University Sheraton. The brochure will be coming shortly. If you would like further information, please call 315-464-7078.

## CNYPCC TIDBITS:

Toxic Odors - Match

| | |
|---|---|
| A. Phosgene | 1. Rotten eggs |
| B. Hydrogen sulfide | 2. Freshly mowed hay |
| C. Cyanide | 3. Vinyl (New car or shower curtain) |
| D. Placidyl (ethchlorvynol) | 4. Bitter almond |

## TOX TRIVIA:

1. What plant does digoxin come from?
2. What plant does colchicine come from?
3. What plant does aspirin come from?

## Case History

**Contributed by:** Jeffrey Spatz, MD, Christine M. Stork, Pharm.D., ABAT

### SEVERE METABOLIC ACIDOSIS

**Case:**

A 39 year old female presents to the Emergency Department after being found unconscious by family members up to 2 days prior to presentation. Initial vital signs include: temperature, 29.5 Celsius (rectal); heart rate, 100 beats per minute; respiratory rate, 20 breaths per minute; blood pressure, 139/86 mmHg. Physical examination was significant for depressed mental status, unresponsive to deep pain. Pupils were 4-5 mm and minimally reactive. Initial laboratory testing revealed sodium of 150 mEq/L, chloride of 115 mEq/L, bicarbonate of <5 mEq/L, BUN of 29 mg/dL, creatinine of 3.6 mg/dL and glucose of 130 mg/dL. An arterial blood gas returned: pH 6.66, pCO2 24, pO2 457. Other significant findings included a measured serum osmolarity of 329 mOsm and a lactate of 7.4 mmol/L.

**What is the differential diagnosis of an anion gap metabolic acidosis?**

This patient is exhibiting an increased anion gap metabolic acidosis with an extremely low pH of 6.66. The normal range for an anion gap calculated from electrolytes measured in the serum is approximately 9-14 depending on how precisely chloride can be measured in the laboratory. (See figure 1 for calculation) This patient's anion gap is 30-35. As the bicarbonate is lowered from a normal value of 24 mEq/L, the acidosis is metabolic.

**Figure 1 - Calculation of the Anion Gap**

**Anion Gap = Sodium - (Chloride + Bicarbonate)**

The differential diagnosis for an anion gap metabolic acidosis can be easily remembered using the mnemonic MUDPILES. (See Table 1)

**Table 1 - MUDPILES**

**M** methanol
**U** uremia
**D** diabetic ketoacidosis (DKA), alcoholic ketoacidosis (AKA), starvation ketoacidosis (SKA)
**P** paraldehyde, phenformin (or metformin)
**I** iron, isoniazid
**L** lactic acidosis (cyanide, H2S, CO, MetHb)
**E** ethylene glycol
**S** salicylates

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**Is there a significant change in the differential diagnosis when the patient has a pH less than 6.9?**

We reviewed the medical literature for case reports of patients presenting with a pH of less than 6.9. Fifty published case reports were found from 1966 to present. Of these 50 cases, 41 were reportedly due to a toxic exposure and 27 (54% of all) involved the ingestion of ethylene glycol or methanol. (See Table 2). Of the 9 non-toxicologic cases, 5 were due to diabetic ketoacidosis.

**TABLE 2 – Cases of Severe Acidosis**

| Toxic Cases w/pH < 6.9 | Non-toxic Cases w/pH <6.9 |
|---|---|
| 17 methanol | 5 diabetic ketoacidosis |
| 10 ethylene glycol | 2 uremia |
| 7 phenformin | 1 sepsis with lactate of 36.7 |
| 3 salicylate | |
| 2 pentaborane | 1 ruptured tubal pregnancy |
| 1 isoniazid | |
| 1 ibuprofen | |

**What is the differential diagnosis for an increased osmol gap?**

The osmol gap is the difference between the calculated osmolarity and the measured osmolality. Here, it is imperative that osmolality be measured using freezing point depression, not boiling point elevation. The latter method may result in a falsely normal measured osmolality due to volatilization of the alcohol. Osmolarity is calculated through various methods. The most commonly used equation is seen in Figure 2: The "normal" osmol gap in emergency department patients reportedly ranges from (-14 to +10). Common causes of an increased osmol gap include toxicologic causes (alcohols, mannitol) and non-toxicologic causes (sepsis, renal failure). A large osmol gap can be quite useful in suggesting the presence of a toxic alcohol in a patient who is not hospitalized with another severe life-threatening injury. However, a small osmol gap is not useful to exclude a toxic alcohol because the alcohol's contribution to the osmol gap may be hidden within the normal range. For example, this patient's osmol gap was calculated at 11.4. If the patient's osmol gap prior to the ingestion of the alcohol was –14, the patient could potentially have a measured methanol level of 80 mg/dL and ethylene glycol level of 155 mg/dL, both requiring emergency treatment.

**Figure 2 - Calculation of Osmolarity**

$$\text{Osmolarity} = (2)\text{Na(mEq/L)} + \frac{\text{BUN(mg/dL)}}{2.8} + \frac{\text{Glucose(mg/dL)}}{18} + \frac{\text{Alcohol}}{R}$$

R = ethanol 4.6, methanol 3.2, ethylene glycol 6.2

**How do methanol and ethylene glycol cause toxicity?**

Methanol, found commonly in dry gas and windshield washer fluid, and ethylene glycol, commonly found in antifreeze, are both alcohols that are sequentially metabolized by alcohol dehydrogenase and aldehyde dehydrogenase to form toxic metabolic products. (See Figure - 3) Methanol forms formic acid, which is responsible for the anion gap acidosis and is also toxic to the retina, ultimately resulting in blindness. Patients, if awake, may complain of a snow field vision as vision is becoming impaired. If unconscious, a pale or hyperemic optic disk may be appreciated on funduscopy.

The primary acid produced after ethylene glycol exposure is glycolic acid and secondarily glyoxylic acid. This is subsequently metabolized to oxalic acid, which binds with calcium to form calcium oxalate crystals. These crystals precipitate most commonly in the urine causing renal failure. Early after ethylene glycol exposure, patients may have fluorescent urine when visualized under a Woods lamp due to an additive, fluorescein, which is included in some antifreeze solutions. Also, calcium oxalate crystals can be visualized in the urine of some patients, although the absence of this finding does not exclude toxicity.

**Can ethylene glycol cause a lactic acidosis?**

Although not formed directly, lactic acid can accumulate after large exposures. This occurs because ethylene glycol metabolism results in a higher than usual NADH to NAD ratio which in turn favors the formation of lactate from pyruvate.

**How are patients with methanol and ethylene glycol ingestions treated?**

Both ethanol and fomepizole are used to prevent the formation of more toxic metabolic products through inhibition of alcohol dehydrogenase activity. (See Figure - 4) Fomepizole is given as a weight based standard dose. Intravenous or oral ethanol is dosed to achieve an ethanol level of 100-200 mg/dL which should then be continuously titrated. It is important to note that should the patient require hemodialysis, both fomepizole and ethanol dosing should be increased during the procedure as both are dialyzable. Advantages of fomepizole over ethanol include ease of administration, lack of blood level monitoring, and lack of significant adverse effects. The major disadvantage is significantly increased cost over ethanol.

Definitive therapy includes hemodialysis which removes both parent toxic alcohol and the toxic metabolites. Most commonly available alcohols have small molecular weights, low lipophilicity, low volumes of

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distribution, and are not ionized which make them extremely amenable to extracorporeal removal. Hemodialysis should be performed for patients with significant acidosis, end organ toxicity or methanol or ethylene glycol levels greater than 25 mg/dL in the absence of toxicity.

**Is there any ancillary therapy that may be beneficial?**

Methanol poisoned patients may benefit from folic acid or folinic acid administration to foster metabolism of formic acid to a non-toxic metabolite. Similarly, thiamine and pyridoxine may enhance the detoxification of glycolic acid after ethylene glycol exposure. Alkalinization using sodium bicarbonate should be used for severely acidotic patients to prevent consequences of severe acidemia. In addition, sodium bicarbonate may be useful in decreasing retinal toxicity seen after methanol poisoning.

**Case Outcome:**

The patient received multiple doses of sodium bicarbonate and emergent hemodialysis due to severe acidosis and complete renal failure. After 2 days, the patient regained mentation but had residual renal failure requiring long term hemodialysis. A presumptive diagnosis of ethylene glycol poisoning was made due to acidosis, renal failure, multiple oxalate crystals in the urine and the patient admitting to ingesting ethylene glycol. The ethylene glycol level on presentation was negative indicating conversion to the toxic metabolic products was complete upon presentation.

Figure 3

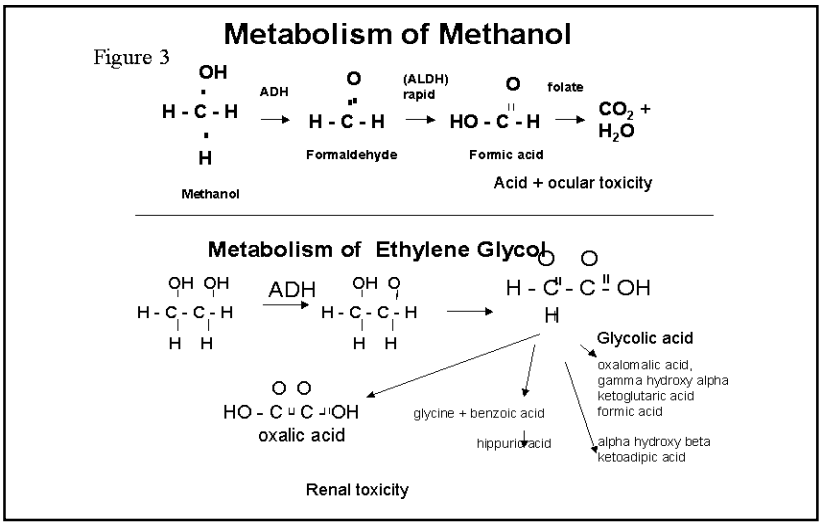
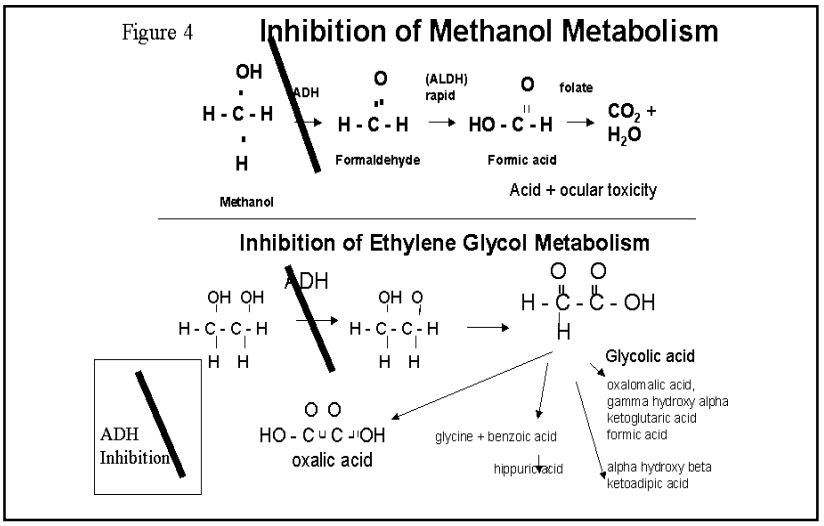



Figure 4




**Select References:**

Brendt J et al: Fomepizole for the treatment of methanol poisoning. N Engl J Med 2001;344:424-429.

Brendt J et al: Fomepizole for the treatment of ethylene glycol poisoning. N Engl J Med 1999;340:832-838.

Kowalczyk et al: Ethanol treatment in ethylene glycol poisoned patients. Vet Human Toxicol 1998;40:225-228.

Jacobsen D et al: Methanol and ethylene glycol posioning, mechanism of toxicity, clinical course, diagnosis and treatment. Med Toxicol 1986;1:309-334.

**CNYPCC Tidbits answers:**

A. 2
B. 1
C. 4
D. 3

**Tox Trivia answers:**

1. Digitalis lantana (Foxglove)
2. Autumn Crocus
3. Bark of the Willow tree

## SPI CORNER TOPIC: "HEADS UP" TO LEAD POISONING

**Contributed by:** Maureen Famiglietti, Lead Program

A 2 year old Sudanese child presented to the ED with a chief complaint of low grade fever and vomiting for one day. The child and family had arrived 3 weeks earlier from an Egyptian refugee camp. Physical examination was non-contributory. Laboratory analysis revealed a microcytic anemia with occasional basophilic stippling. A streptococcus antigen test was positive and the patient was sent home with antibiotics. Twenty three days later, the chid expired. The lead level returned at 391 mcg/dL.1,2

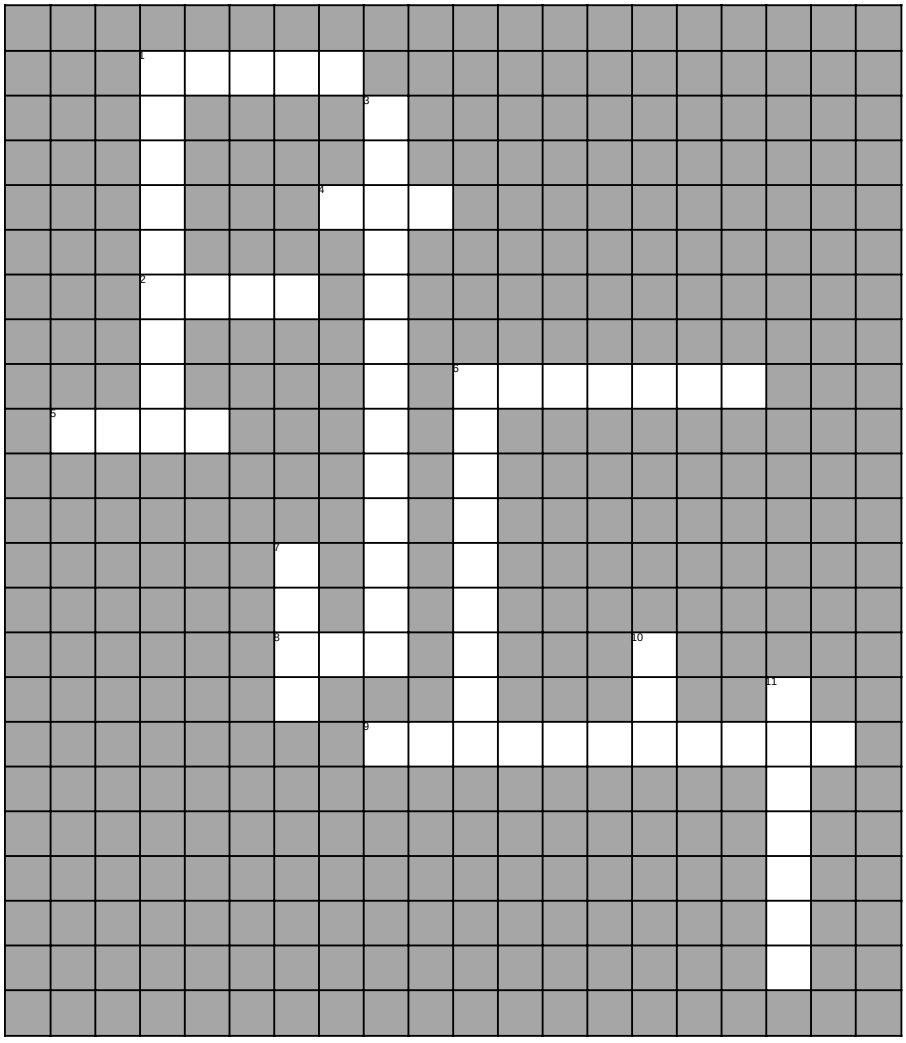
Intensive investigation by the CDC and Egyptian authorities revealed that a great amount of the exposure occurred during the 5 weeks she was in the US. This child's death, the first in the US in 10 years attributed to lead poisoning, reminds us that this environmental hazard continues to threaten children and that severe poisoning can be fatal.

In the emergency department, the following children should be screened for lead exposure:

1. Newly arrived immigrant children (Eastern Europe, China, Africa)
2. Children with a history of an increased lead level
3. Children who live in older, poorly maintained rental housing
4. Children who are not receiving routine well child care

New York State Department of Health requires health care providers to routinely test all one and two year-olds for elevated blood lead levels. The Central New York Lead Poisoning Resource Center, under the direction of Howard L. Weinberger, MD, is available to provide consultation for any child identified with an elevated blood lead level.


1. MMWR 2001;50(22), June 8.
2. Pediatrics 2001;108:158-162.

## MIXED BAG

**Contributed by:** Trudy Dody, RN, CSPI

**Down**

1. What John Belushi died of
3. Author of Silent Spring, not related to Johnny.
6. Weight loss drug.
7. Abbreviation for the organization credited with safety in the workplace.
10. Abbreviation for the treatment for CO poisoning.
11. Antidote for a toxic methanol ingestion.

**Across**

1. Chemical warfare agent used in the 1995 Tokyo subway bombing.
2. Poisonous toad.
4. The leading cause of death in the US according to Poison Control Centers.
5. Another word for obtunded
6. Appearance of pupils after ingesting ephedrine.
8. Abbreviation for one of the vital sign changes seen after sympathomimetic ingestions.
9. Active ingredient in chocolate

Answers:

Down 1. Speedball, 3. Rachael Carson, 6. Dexedrine, 7. OSHA, 10. HBO, 11. Antizol
Across 1. Sarin2. Bufo, 4. TCA 5. Dull, 6. Dilated, 8. HTN, 9. Theobromine