

Central
New York
Regional
Poison
Control
Center

The CNYPC

January, 2001

Toxicology Letter

Vol. VI No. 1

A Quarterly Publication

SCHEDULED EVENTS:

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

January 10, 2001
February 14, 2001
March 14, 2001

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

PROGRAM ANNOUNCEMENT:

We hope you all enjoyed the Fourth Annual Toxicology Teaching Day. If you would like a syllabus, please call 315-464-7078. Information on our Fifth Annual Toxicology Teaching Day will be coming shortly. Stay Tuned.

CNYPC TIDBITS:

1. A potassium of \geq (____) indicates a potential for lethality after ACUTE digoxin overdose.
2. Potassium does not have prognostic value after CHRONIC digoxin overdose. (True/False)
3. Digoxin level after the administration of digoxin specific Fab fragments is of no value as it is measuring both free digoxin and digoxin bound to digoxin specific Fab fragments. (True/False)

TOX TRIVIA:

Match the toxin with the major organ affected

- | | |
|-------------------------|-----------|
| 1. Toluene | A. Kidney |
| 2. Carbon tetrachloride | B. Heart |
| 3. Chronic ipecac | C. Liver |

Case History

Contributed by: Jayne Healey, M.D.
Christine M. Stork, Pharm.D. DABAT.

BREATHLESS FARMERS AND HOCKEY PLAYERS

Case:

A 54 year old previously healthy male presented to the emergency department complaining of 4 hours of increasing dyspnea. Initial vital signs included a temperature of 102° F, heart rate of 90/minute, blood pressure of 130/80 mmHg, respiratory rate of 30/minute, and pulse oximetry of 93% on 3 liters/minute of supplemental oxygen by nasal cannula. The physical examination was significant for rales in the lower two-thirds of the lungs bilaterally. An arterial blood gas (ABG) analysis revealed a pH of 7.40, pCO₂ of 38, pO₂ of 66, base excess of negative 23, and an A-a gradient of 0.45 on 3 liters nasal cannula. The patient subsequently vomited and became hypotensive, requiring IV fluid resuscitation. History revealed that he had been working in his silo earlier in the day.

What is "Silo Filler's disease"?

"Silo filler's disease" is a term used to describe a syndrome of acute pulmonary toxicity experienced by farmers exposed to high levels of nitrogen dioxide (NO₂) while working in silos. Silos that house decomposing fertilizer accumulate toxic levels of nitrogen dioxide if not properly ventilated. At very high levels, the gas is seen as a reddish-brown haze and has a bleach-like odor. Due to its low water solubility, nitrogen dioxide is only mildly irritating to the upper airways, therefore prolonged exposure and inhalation deep within the lungs is possible. Symptoms are typically delayed and consist of cough, dyspnea, chest pain, nausea, and vomiting. Patients often present with hypoxia and may appear cyanotic. Nitrogen dioxide has direct toxicity against pulmonary tissues, reducing available surfactant. Nitrogen dioxide also generates free radicals, causing further alveolar injury. In addition, dissolution of NO₂ in the water of the respiratory tract forms nitric and nitrous acids, also damaging to pulmonary tissues. Significant exposure results in pulmonary edema and pneumonitis. In a small subset of patients, enough NO₂ is converted to nitrates to cause methemoglobinemia. Chest x-rays in exposed patients reveal diffuse infiltrates in a miliary pattern or confluent opacities consistent with pulmonary edema.

Where else is nitrogen dioxide found?

Nitrogen dioxide is found in detectable levels as a result of air pollution and may contribute to chronic lung diseases such as asthma. It is a byproduct of welding and brazing processes and is also

BREATHLESS FARMERS AND HOCKEY PLAYERS

produced during the burning of radiographic film. Patients trapped in closed-space fires may have significant exposures to NO₂. Interestingly, ice-cleaning machines, such as the Zamboni, oxidize propane and produce NO₂ as an end-product. The enclosed space of an ice arena may become a dangerous source of NO₂ exposure. Several literature reports cite cases of hockey players developing pulmonary symptoms consistent with NO₂ toxicity after prolonged periods of time spent in ice arenas maintained by Zambonis.

What are some other toxic gases?

Toxic gases are categorized into two large groups. The simple asphyxiant gases generally possess no direct toxicity but simply reduce the partial pressure of available oxygen by displacement, lowering the concentration to less than 21%. The ultimate effect of these gases is to induce hypoxemia in poisoned patients. Treatment consists of removal from exposure, supplemental oxygen, and ventilatory assistance, if necessary. Gases falling into this category include: the noble gases helium, neon, argon, and xenon; hydrocarbons such as methane, ethane, propane, and butane; and also carbon dioxide and nitrogen.

The irritant gases, in addition to displacing oxygen, cause direct damage to the respiratory tract. Whereas asphyxiant gases are more insidious in their presentation of progressive dyspnea, irritant gases often cause immediate symptoms related to mucosal irritation. Rapidity of onset of symptoms is related to the hydrophilic nature of the individual gases, as will be discussed below. Hypoxemia results, not from reduction of pO₂, but from destruction of pulmonary tissues with subsequent compromise of gas exchange.

What are the irritant gases - and how are they classified?

Irritant gases require dissolution in mucosal water in order to exert their toxic effects. The water solubility of an irritant gas determines its likelihood of causing pulmonary damage. Highly water soluble gases dissolve rapidly and cause immediate symptoms of conjunctival, nasal, oral, and pharyngeal irritation. Victims tend to remove themselves promptly from exposure and avoid inhalation deep within the lungs. These agents typically produce only upper respiratory tract damage. Exceptions occur when patients are exposed to very high concentrations or if there is a delay in escape.

Gases with very low water solubility are less rapidly irritating, and patients may not recognize symptoms until significant exposure has occurred. Prolonged breathing of the irritant gas increases not only the level of exposure but also the depth of entry into the bronchopulmonary system. Inflammatory responses to these agents consist

(CONT.)

of tracheobronchitis, bronchiolitis, and pulmonary edema. When alveolar damage with subsequent impaired diffusion capacity occurs, patients exhibit significant morbidity and mortality.

What are the clinical manifestations of exposure?

Patients exposed to highly water soluble irritant gases may present with pain and mucosal edema of the eyes, nose, and throat, chemosis, drooling, cough, and stridor. Dermatologic irritation is also common with this group. These symptoms are typically immediate in onset after exposure.

Gases with intermediate water solubility share characteristics with gases of both the low and high water solubility groups. They produce less rapid mucosal irritation, thus inhalation further into the bronchopulmonary system is possible. Symptoms of both upper and lower respiratory tract irritation (throat pain, cough, dyspnea, etc) tend to progress over 6-8 hours.

Victims of poisoning with gases of low water solubility present less acutely but have a higher risk of progression to more serious disease. Initial symptoms may consist only of mild dyspnea and cough. Delayed symptomatology includes extreme dyspnea, chest pain, nausea and vomiting, and cyanosis. On physical exam, rales or wheezes can be noted. Pulse oximetry and laboratory analysis may reveal severe hypoxemia. Chest x-rays may show diffuse interstitial infiltrates or an alveolar pattern consistent with pulmonary edema. The most severe and dreaded form of this injury is acute respiratory distress syndrome (ARDS). Mortality from this syndrome is as high as 30%.

What is the initial patient management?

With any of the irritant gas exposures, immediate removal from the source is critical. No "antidote" exists for any of these agents, and treatment remains primarily supportive. Any patient with significant exposure should be admitted to the hospital for observation, despite initial mild symptomatology. Progression to more severe disease should be anticipated. Supplemental oxygen is recommended for all irritant gas exposures. Bronchodilation with inhaled β -agonists is useful in relieving bronchospasm. Patients who fatigue or are unable to maintain their oxygenation should be intubated with mechanically assisted ventilation.

Victims with brief exposures to irritant gases with high water solubility, after initial management, require no further medical treatment. Symptoms are self-limiting, and delayed manifestations are not typical.

Patients with toxic inhalations of intermediate solubility gases warrant observation for 6-8 hours after exposure. They may initially present with mild clinical manifestations

BREATHLESS FARMERS AND HOCKEY PLAYERS

but later progress to more severe symptomatology. Some agents, such as chlorine gas, are converted to acids on exposure to water and are extremely caustic to mucosal tissues. Aerosolized sodium bicarbonate, diluted to 2%, is warranted if symptoms of irritation persist.

Treatment of low water solubility irritant gas poisoning consists of ensuring adequate oxygenation and ventilation, as described above. All patients should be admitted to the hospital for observation, as symptoms are likely to progress over 12-24 hours. Corticosteroids are controversial but are shown to be of some benefit in select patients. Methemoglobinemia resulting from nitrogen dioxide conversion to nitrates is treated with methylene blue. Possible late sequelae of toxic exposure are fibrotic changes in damaged airways resulting in bronchiolitis obliterans. Here, patients present 2-6 weeks after initial exposure with signs and symptoms similar to their initial presentation. Corticosteroids may be beneficial in preventing and treating these complications

Ensure adequate patient follow-up.

Patients must be counseled to follow up closely with their primary medical doctor after significant exposure to low water solubility irritant gases. As mentioned previously, inflammatory responses in the pulmonary tissues may result in delayed sequelae of fibrotic changes in the lungs. Patients should be made aware that there could be a latent phase of 2-6 weeks during which they are asymptomatic, followed by acute relapse of symptoms similar to their initial presentation. They should be instructed to seek medical care for recurrence of dyspnea, cough, and/or fever. Bronchiolitis obliterans and pulmonary edema are also possible after the latent phase, even despite initial mild clinical manifestations. Again, corticosteroids are controversial but may be helpful in preventing long-term pulmonary fibrosis.

Maintaining a high index of suspicion.

A high index of clinical suspicion is required when assessing patients with acute onset of dyspnea. Otherwise healthy patients with no past medical history of pulmonary disease warrant evaluation for possible toxic gas poisoning. Eliciting an in depth history may reveal

CNYPCC Tidbits answers:

1. 5 mEq/L (100% fatality if greater than 5.5 mEq/L)
2. True
3. True

Tox Trivia answers:

1. A
2. C
3. B

(CONT.)

exposure that the patient is unaware of. During the fall and winter months, awareness of common irritant gases may yield a diagnosis when the history doesn't seem contributory. As the title suggests, farmers filling silos and hockey players exposed to Zamboni fumes typically present in the fall or winter with acute onset of dyspnea. In these cases, keep nitrogen dioxide on the list of differential diagnoses while ruling out other cardiac and pulmonary etiologies.

Case follow-up.

The patient was admitted to the ICU and continued to require O₂ at 3 L/min by nasal cannula in order to keep pulse oximetry above 90%, but he never required intubation or mechanical ventilation. His vital signs corrected to a temperature of 99.2o F, heart rate of 79/minute, blood pressure of 120/80, and respiratory rate of 18/minute. The next day his lung exam revealed only moderate bibasilar rales, he no longer required supplemental oxygen, and his chest x-ray showed resolving interstitial edema. The patient was able to be discharged home after 2 days, but close follow-up with his physician for several weeks was recommended in order to monitor for late sequelae.

Table 1. Classification of common irritant gases - solubility in water

High Solubility	Intermediate Solubility	Low Solubility
Chloramine	Chlorine	Phosgene
Ammonia	Ozone	Nitrogen dioxide

Suggested Reading:

1. Anonymous. Ice hockey lung: NO₂ poisoning. Lancet. 1990; 335(8699):1191.
2. Douglas, WW, Hepper, NG, Colby, TV. Silo-filler's disease. Mayo Clinic Proceedings. 1989; 64(3):291-304.
3. Goldfrank, et al. Toxicologic Emergencies, 6th ed.. 1998. Chapters 94 and 110.
4. Karlson-Stiber, C, Hojer, J, Sjöholm, A, Bluhm, G, Salmonson, H. Nitrogen dioxide pneumonitis in ice hockey players. Journal of Internal Medicine. 1996; 239(5):451-6.
5. Rorison, DG, McPherson, SJ. Acute toxic inhalations. Emergency Medicine Clinics of North America. 1992; 10(2):409-35.
6. Zwemer, FL, Jr, Pratt, DS, May, JJ. Silo filler's disease in New York State. American Review of respiratory Disease. 1992; 146(3):650-3.

SPI CORNER TOPIC: NEWSWORTHY FDA CHANGES

Contributed by: Marvleen Hollenbeck, R.N. CSPI

Troglitazone

In March 2000, the manufacturer of Rezulin ® (troglitazone) was asked by the FDA to remove this drug from the market. Parke-Davis/Warner-Lambert agreed to the request. This action was based on the FDA's review of safety data on Rezulin ®, a drug used to treat type 2 diabetes. Two similar drugs, rosiglitazone (Avandia®) and pioglitazone (Actos®) were also investigated, but it was found these two were less toxic to the liver than Rezulin ®. Recent safety data demonstrates that Actos ® and Avandia ® offer the same benefits as Rezulin ® but not the same risks.

Since 1997, Rezulin ® has been known to cause severe liver toxicity. At that time, Park-Davis strengthened the label warning and advised close monitoring of liver function in patients on Rezulin ®. The adverse effects were studied and it was made clear that the newer drugs had less risk of liver toxicity.

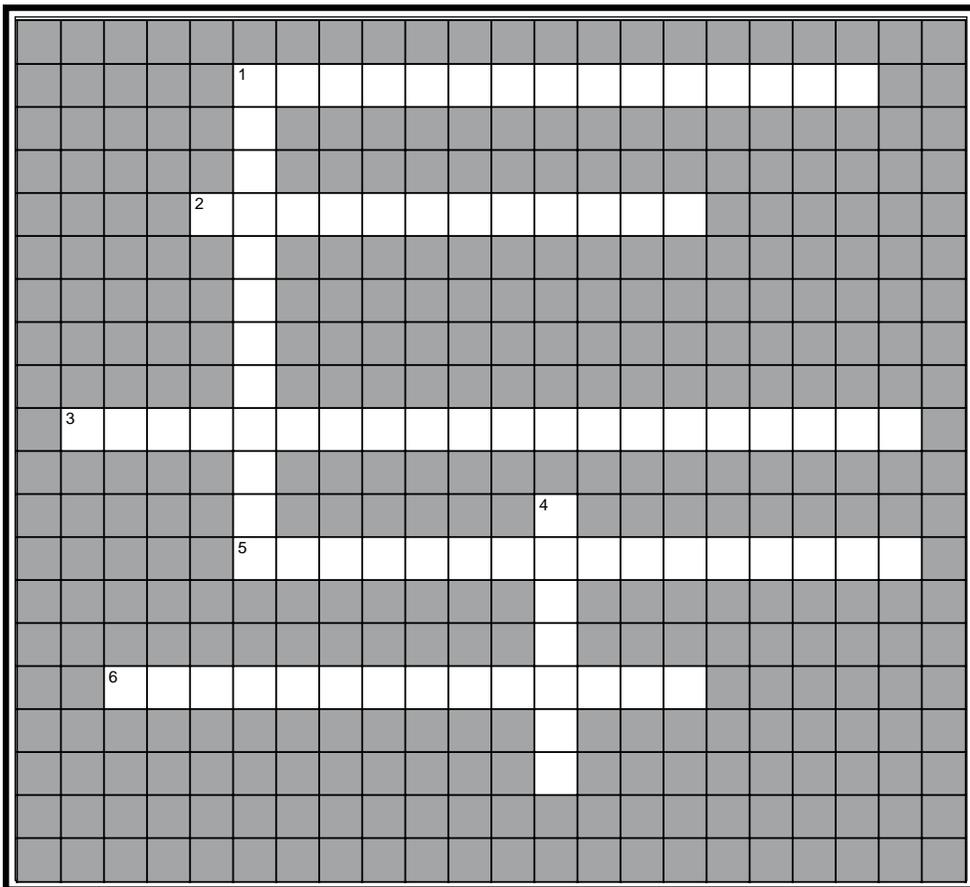
Phenylpropanolamine (PPA)

On November 6, 2000, the Food and Drug Administration (FDA) produced a public health advisory concerning the risk of hemorrhagic stroke while using

phenylpropanolamine hydrochloride. It is now requested that drug companies discontinue marketing products containing PPA. This drug is an ingredient in many over-the-counter cold and cough medications and also in OTC weight loss products.

The new warning was issued based on information that was provided to the FDA from scientists at Yale University School of Medicine. Their report entitled "Phenylpropanolamine and Risk of Hemorrhagic Stroke: Final Report of the Hemorrhagic Stroke Project" found that women had an increased risk of stroke but men may also be at risk after PPA use.

The FDA plans to remove PPA as an ingredient in over-the-counter and prescription drug products but until then recommends that consumers not use any products use products that contain PPA. It is included in such brand name products as Triaminic ®, Dimetapp ®, Coricidin ®, Contac Maximum Strength ®, Comtrex ®, Tavist-D ®, Triaminicol Multi-Symptom ®, Acutrim ®, Dexatrim ® and Stay Trim Diet Gum ®, along with many others. Local stores have started pulling these products from their shelves. If possible, many of these products may be reformulated without PPA and then returned to the market.



DRUGS CAUSING TACHYCARDIA

Contributed by:
Teesh Guenther, RN, CSPI

Across:

1. Diphenhydramine, antipsychotics, antispasmodics, some plants
2. Bronchodilator, COPD treatment
3. Examples: imipramine, doxepin
5. albuterol, epinephrine, cocaine
6. examples: Mellaril ®, Serentil ®, Prolixin ®

Down

1. used for ADD, used for weight loss
3. "nicknames" crack, snow

Across: 1. anticholinergic; 2. theophylline; 3. cyclic antidepressants; 5. sympathomimetics; 6. phenothiazines
Down: 1. amphetamines; 4. cocaine



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Health Sciences Library Room 318
Second Wednesday of the Month, 11:00 AM

April 11, 2001, 11:00 AM

May 9, 2001, 11 AM

June 13, 2001, 11 AM

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

PROGRAM ANNOUNCEMENT:

The Fifth Annual Toxicology Teaching Day will be held on November 7, 2001 at the University Sheraton.

A flyer will be coming shortly. If you would like advance information, please call 315-464-7078.

CNYPC TIDBITS:

Toxic Alcohols – Match to the Alcohol

- | | |
|-------------------------------|-----------------------------|
| A. methanol | 1. renal failure |
| B. isopropanol | 2. ketosis without acidosis |
| C. ethylene glycol | 3. ocular toxicity |
| D. propylene glycol formation | 4. lactic acid |

TOX TRIVIA:

1. What is the toxin responsible for Woolsorter's disease?
2. What was the toxin released in Bopol?
3. What homicidal poison is associated with burning toes, hair loss and multi-system organ failure?

Case History

Contributed by: T. Michele Caliva, RN, CSPI, Christine M. Stork, Pharm.D., ABAT

DILEMMA IN GASTROINTESTINAL DECONTAMINATION

Patients who are exposed to a toxin require a thorough initial assessment before appropriate management decisions can be made. The assessment should include:

- Evaluation of airway, breathing and circulation
- Assessment of mental status and r/o hypoglycemia
- ECG, including QRS measurements, especially in acute overdoses to r/o exposure to tricyclic antidepressants or other sodium channel antagonists
- Patient and exposure history
- Physical exam and routine baseline labs
- Toxidrome identification.

Once the patient assessment is completed and immediate life-saving interventions have been performed, it is time to consider the role of gastrointestinal decontamination. The goal of gastrointestinal decontamination is to remove a harmful substance from the body before it can be absorbed and cause systemic toxicity. Currently available methods of gastrointestinal decontamination include syrup of ipecac, orogastric lavage, activated charcoal, and whole bowel irrigation. We will address the appropriate use of the various gastrointestinal decontamination methods available using case demonstrations.

Case A: A 40-year-old unresponsive male is brought to the Emergency Department via ambulance. An empty bottle of # 100 Aspirin 325 mg tablets, as well as empty bottles of various cold medications were found in the patient's home.

Case B: A 16-year-old male presents to the Emergency Department after ingesting an unknown amount of Benadryl and 2 beers.

Orogastric Lavage

Orogastric lavage is most effective early after exposure, preferably within 1 hour, but is also useful later in cases where residual drug may be in the stomach. Orogastric lavage should be accomplished using the largest tube possible (40 F in adults and 24-28 French in children). With the patient in the left lateral decubitus position and airway adequately protected, normal saline (200-300 mL in adults and 10 mL/kg in a child) is instilled and withdrawn at regular intervals until the fluid is clear. Orogastric lavage should not be considered in patients who have ingested a toxin that is easily aspirated, such as a hydrocar-

DILEMMA IN GASTROINTESTINAL DECONTAMINATION

bon, is corrosive to the gastrointestinal tract (there are some exceptions), or when there is a medical or surgical condition compromising the integrity of the gastrointestinal tract. Complications of orogastric lavage include aspiration pneumonia, injury to the throat, stomach, or esophagus, or fluid and electrolyte imbalance. Studies in healthy subjects find that the amount of a given substance removed via orogastric lavage varies from 32% to 8% depending on the substance. Factors that influence the efficacy of lavage include: toxin location in the gastrointestinal tract, size of pills or substances ingested, and the size of lavage tube. Large trials in poisoned patients failed to demonstrate a change in outcome for the majority of patients treated with orogastric lavage vs. activated charcoal alone. As a result, orogastric lavage is now reserved for patients who, by history or physical examination, are thought to have ingested a life-threatening amount of a toxin. Case A meets this criteria because of the dose ingested, while case B does not.

Case A: A 2-year-old female is playing in the backyard with her father. She picks up a mushroom and eats it. Dad witnesses the ingestion and attempts to remove the mushroom from her mouth. He is able to remove some but the child swallows most of it.

Case B: An 18 month old boy reaches up on the counter and drinks 3 ounces of acetaminophen liquid from an open container. The amount ingested was calculated to be 180mg/kg.

Syrup of Ipecac

Syrup of Ipecac is derived from the roots of *C. acuminata* or *C. ipecacuanha*. The active components of these plants are the alkaloids, cephaline and emetine. Syrup of ipecac produces vomiting through both direct irritation, and through stimulation of the chemoreceptor trigger zone (vomiting center) in the brain. The dose is 30 mL in adults, 15 mL for children 1-12 years of age and 10 mL for children 6 months to 1 year of age. Emesis is expected in 20-30 minutes and the dose can be repeated once. Similar to orogastric lavage, syrup of ipecac removes approximately 30% of a toxin if administered within the first hour after ingestion. Also, similar to orogastric lavage, studies do not demonstrate a change in outcome due to administration of syrup of ipecac in the majority of cases. The inability to use syrup of ipecac in patients with a potential for a change in mental status, seizures, or where an oral antidote will be effective has led to its diminished use. Syrup of ipecac may be of some value in the scenario described in Case A, where the ingestion is early and witnessed, and there is a potential for delayed toxicity which may be life threatening. In Case B, the use of syrup of ipecac would not be indicated because this patient has taken a toxic amount of acetaminophen (above 150mg/kg) which requires

(CONT.)

activated charcoal and may also require oral antidote administration.

Case A: A 29-year-old female presents to the ED after ingesting several 500mg acetaminophen tablets. She states that the ingestion occurred 1 hour ago.

Case B: A five-year-old male and his 3-year-old sister present to the ED after ingesting several pre-natal vitamins with iron.

Single Dose Activated charcoal (SDAC):

Activated charcoal is a black odorless powder that is produced from wood or coconut that is burned and then treated with steam or carbon dioxide. It is available both in the powder or aqueous form. It is the latter form that is most often used in the healthcare setting. The dose of AC is 1 g/kg orally which is the largest, well-tolerated dose in most patients. Activated charcoal adheres to toxins in the gastrointestinal tract, thereby preventing absorption into the body and thus preventing systemic toxicity. It is most effective when administered early where it is more likely to reach the toxin in the gastrointestinal tract, but continues to be of use later in select circumstances. Some toxins, such as alcohols, heavy metals, lithium, and iron adhere poorly to activated charcoal, if at all. Activated charcoal should not be administered if there is medical, surgical, or chemical (i.e. caustic ingestion) gastrointestinal compromise. In Case A, administration of activated charcoal is indicated as it is shown to effectively lower anticipated acetaminophen serum concentrations. In Case B, activated charcoal would be of limited value unless a co-ingestant is considered, because it does not bind to iron.

Multiple-Dose Activated Charcoal (MDAC):

Case A: A 50-year-old female presents to the ED after ingesting 20 Valium tablets.

Case B: A 19-year-old male is brought in by ambulance after admitting that he ingested several sustained release Theophylline tablets. Multiple dosing of activated charcoal may be beneficial in those cases where a large amount of a toxin is ingested and it is unlikely that a single dose of activated charcoal (1g/kg) would be enough to result in the desired binding ratio of 10:1 (activated charcoal to drug). In addition, multiple doses of activated charcoal should be considered for those toxins that exhibit enterohepatic metabolism of an active metabolite or those that can exhibit enteroenteric recirculation. The frequency of multiple doses of activated charcoal is determined by the relative efficacy of the activated charcoal in relation to the severity of the anticipated effects of the toxin. Generally, 0.25-2g/kg of activated charcoal can be used every 1-6 hours. Common toxins that exhibit enterohepatic recirculation of an

DILEMMA IN GASTROINTESTINAL DECONTAMINATION

(CONT.)

active metabolite include amitriptyline, carbamazepine, and dapsone. Enteroenteric re-circulation occurs when there is a negative relative concentration of toxin in the gut, and toxin diffuses passively from the mesenteric circulation into the gut lumen and is trapped. Examples of toxins that exhibit enteroenteric recirculation include theophylline, phenobarbital, and phenytoin. Case B would be an example where multiple dosing of activated charcoal is recommended, due to enteroenteric recirculation. Case A does not meet the criteria for multiple dosing of activated charcoal.

Whole Bowel Irrigation (WBI)

Case A: A 14 year old female presents to the ED after ingesting 15 Calan SR tablets.

Case B: A 14 year old female presents to the ED after overdosing on an unknown amount of Paxil 20 mg tablets.

Whole bowel irrigation places large amounts of high molecular weight polyethylene glycol electrolyte solution (PEG solution) that is electrolyte neutral into the gut lumen in an attempt to clear the contents of the gastrointestinal tract in a short amount of time. The appropriate dose of PEG solution in an adult is 2 L/hr and up to 500 ml/hr for children. Continuous administration of the solution should occur until the rectal effluent is clear (4-6 hours). Side effects associated with WBI are limited to nausea, vomiting, and cramping. Contraindications include an unstable patient, obstruction and hemorrhage.

Because WBI does not have much clinical data to support its use, it is reserved for the clearance of those toxins where activated charcoal is not useful either because of adherence properties or because of a large dose of ingested toxin. In addition, the toxin must have slow absorption qualities for it to be effectively removed. WBI is indicated in situations such as Case A, where not only has a sustained release product been ingested, but this drug overdose has potentially life-threatening effects that historically occur despite the use of multiple doses of activated charcoal. In this case, early and aggressive intervention with WBI is indicated. In Case B, a single dose of activated charcoal and supportive care are the only treatment required.

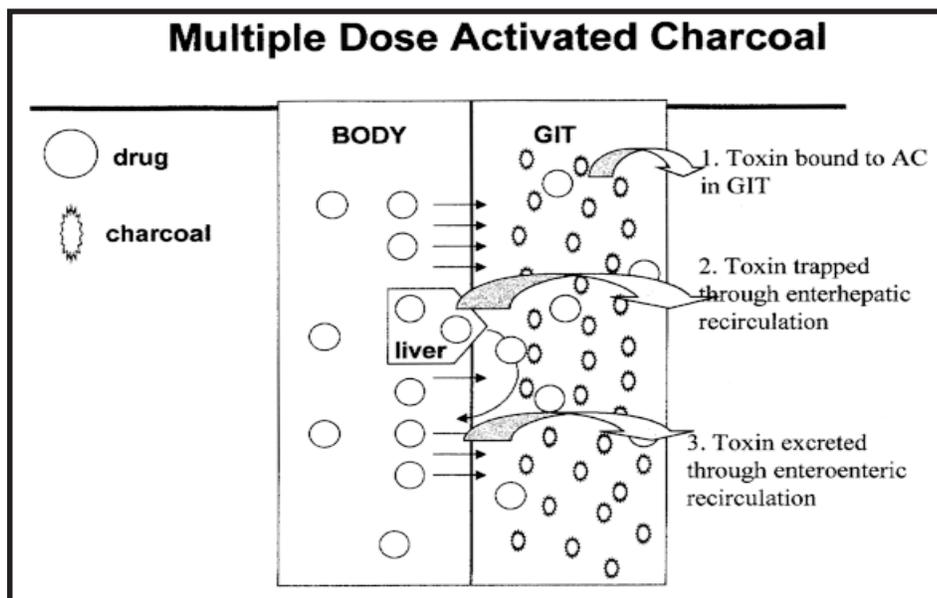
Cathartics:

The effectiveness of cathartics is not well established. No studies demonstrate that cathartics are beneficial after toxin exposure. It is our position that the use of cathartics should be considered rarely and on an individual basis.

References:

Pond SM, Lewis-Driver DJ, Williams GM, et al: Gastric Emptying in acute overdose: a prospective randomized controlled trial. *Med J Australia* 1995;163:345-349.

Kulig K, Bar-Or D, Cantrill SV et al.: Management of acutely poisoned patients without gastric emptying. *Ann Emerg Med* 1985;14:562-567.



CNYPCC Tidbits answers:

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

Tox Trivia answers:

- 1. Anthrax
- 2. Isocyanate
- 3. Thallium (or arsenic)

SPI CORNER TOPIC: "NATURAL" VIAGRA - NATURE'S ANSWER TO IMPOTENCE

Contributed by: Susan Bruce, PharmD Candidate

Anyone can buy "viagra" without a prescription. Although these products do not contain Pfizer's sildenafil - the FDA approved prescription medication, the Viagra craze continues and people will try almost anything. This holds true especially if it is less expensive than paying for an office visit to a physician and a prescription for Viagra.

Following are a few examples of the strategies people are using to sell their products, claiming to achieve the same effects as the real Viagra.

Lebanon's natural version is a wild root, shirsh zallouh, a small shrub with tiny white or yellow flowers and thin leaves. It grows wild in the mountains of Lebanon.

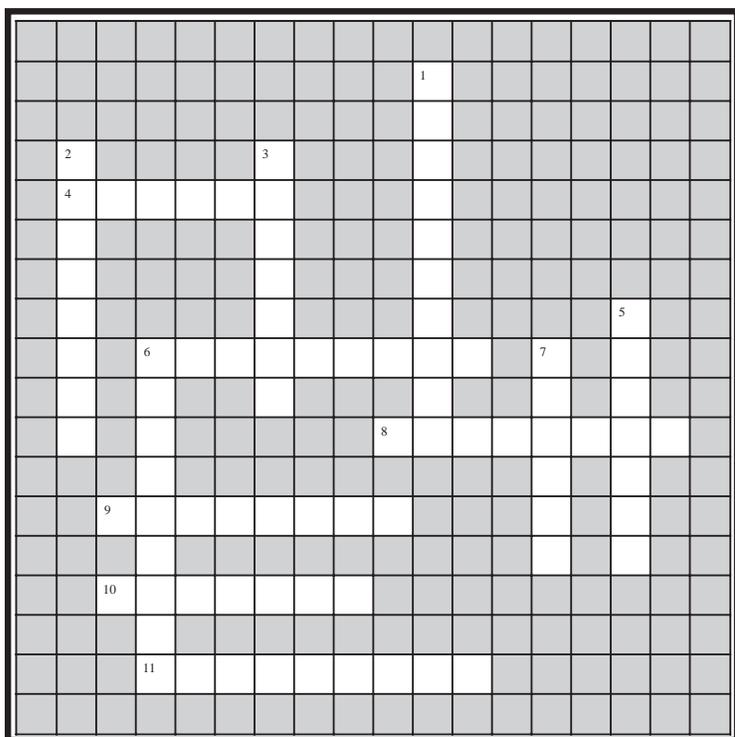
Apparently, shirsh zallouh has been used in Lebanon for generations, but its popularity is becoming worldwide. An extract is made from the root, and a pharmacist in Beirut claims the "taste is a little rough" so it is best to place the drops in milk or juice. Trying to find information about the shrub that this product is from is difficult, let alone its medicinal possibilities. A product called Milagro claims to have all the nutrients essential for "increased desire, enhanced erectile functions, ejaculatory control and improved fertility," even though the actual nutrients are never listed. Lu Rong (also known as Deer Antler Velvet) is a Chinese medicine that has been available for 3000 years. The English translation reveals that the product comes from "the soft velvet-like covering of deer antlers while they are still growing and still in a cartilaginous state, before they harden into bone." Known "ingredients" include calcium, phosphorus, sulfur, magnesium, potassium, sodium, manganese, zinc, copper, iron, selenium, cobalt, the major

amino acids, collagen, anti-inflammatory prostaglandins, gangliosides, natural sex hormones and steroids.

Moving to another part of the globe, Male Plus, the "Amazon Herbal for Men", contains four herbs from the Amazon Rainforest. The main ingredient is extract of Muira puama, which is thought to increase libido and successfully treat "organic- and psychogenic-related impotency." The other ingredients (Catuaba [an aphrodisiac], Sarsaparilla, and Damiana [an aphrodisiac]) work with Muira pauma. Herbal Male Formula is a combination of the following: wildcrafted American ginseng, yohimbe bark, Chinese and Korean ginseng, saw palmetto berries, sarsaparilla root, kola nut, ginger rhizome, Siberian ginseng, juniper berries, and uva ursi leaves. The makers claim use of the product will help men who have lost their "maleness" to "provide more male energy, increase sexual drive and desire, and enhance the male sense of well being."

One last example is androstenedione. Along with stimulation of the user's sex drive, are the usual claims for increases in "muscle size, strength and recovery from exercise."

The reliability of herbal products and their manufacturers for the intended therapeutic claim does not need to be reiterated. However, it is important for us to be aware of what is out there and what people are experimenting with. Until regulation of natural products is a function of the FDA, we need to evaluate the little information available for safety and efficacy. Poor production leading to contaminated products, or misuse of the products could result in harm to the user, which may lead to a call to the poison center.



Across: 4. iodine; 6. clonidine; 8. pillosoc; 10. seldane; 11. ritonavir
Down: 1. cadizensr; 2. kloppin; 3. feidene; 5. codeine; 6. cardenesr; 7. prozac

DANGEROUS SOUND-ALIKES

Medications with similar names are often a source of error

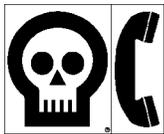
Contributed by: Margo M. Spain

Down

- CCB, Antianginal, antihypertensive and antimigraine
- I'm a benzodiazepine/anticonvulsant. Sometimes I am given for restless legs.
- My generic name is piroxicam. Don't forget food with this pain reliever
- Opiate family found in many antihistamines, decongestants and expectorants
- This antidepressant, SSRI can be fatal if taken with MAOI's
- CCB, antihypertensive and antianginal agent. I relax coronary artery smooth muscle

Across

- NSAID – osteoarthritis. May increase phenytoin and lithium levels.
- Antihypertensive prototype, alpha adrenergic agonist
- Gastric acid pump inhibitor
- Antiviral action against HIV
- Produces less drowsiness than other antihistamines because it does not cross the blood-brain barrier
- Anti-infective antiviral protease inhibitor



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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.

CNYPC 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 osmolality 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

$$\text{Anion Gap} = \text{Sodium} - (\text{Chloride} + \text{Bicarbonate})$$

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
3 salicylate	36.7
2 pentaborane	1 ruptured tubal
1 isoniazid	pregnancy
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

Figure 2 - Calculation of Osmolarity

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

2.8	18	R
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$$R = \text{ethanol } 4.6, \text{ methanol } 3.2, \text{ ethylene glycol } 6.2$$

“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.

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

Continued on Page 3

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.

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.

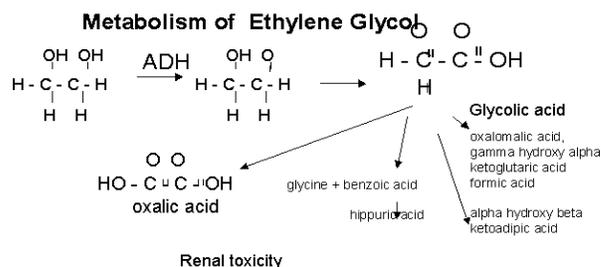
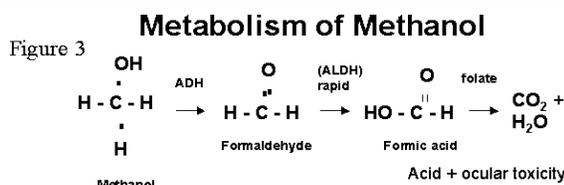
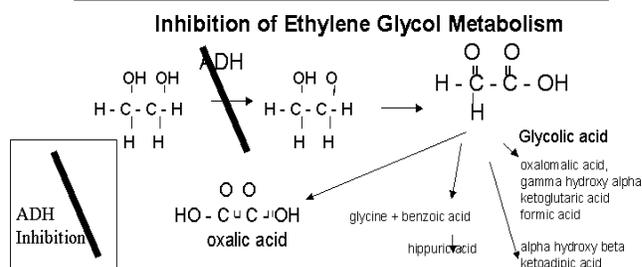
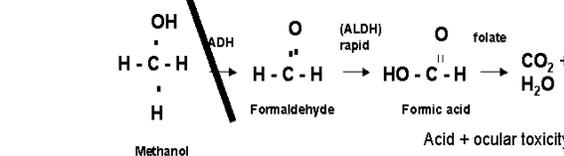


Figure 4 Inhibition of Methanol Metabolism



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 poisoning, 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

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 child expired. The lead level returned at 391 mcg/dL.^{1,2}

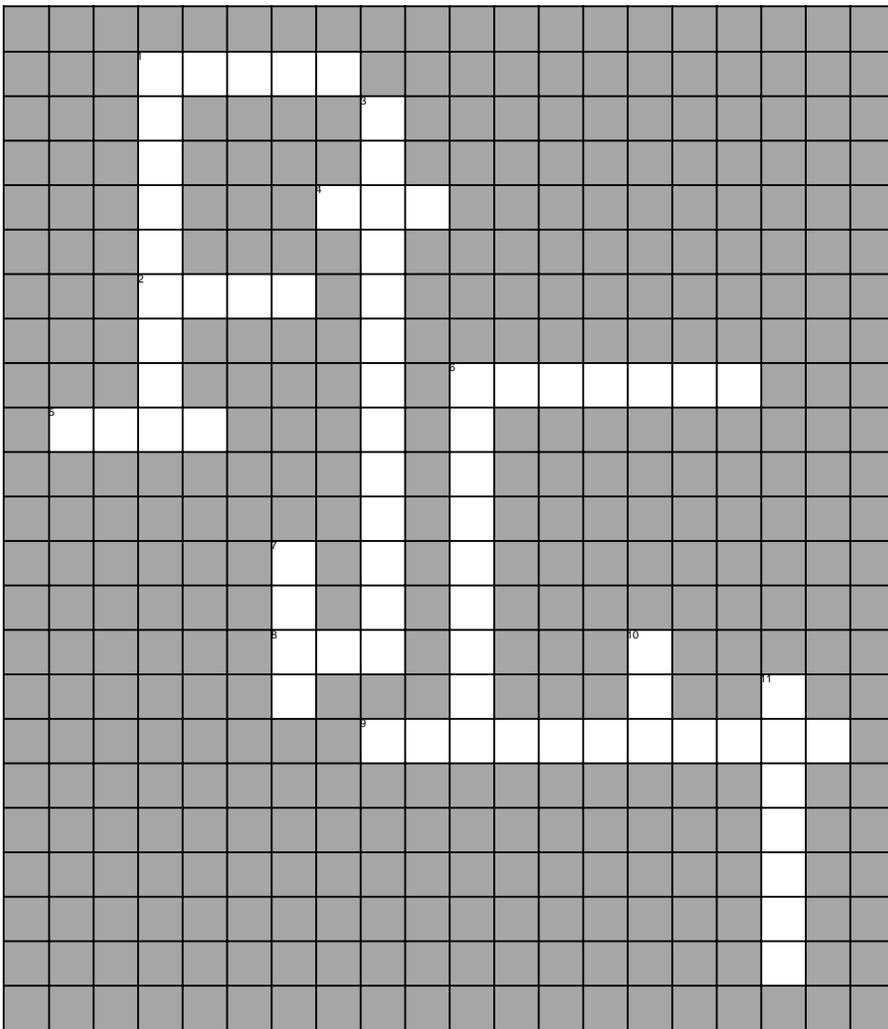
Intensive investigation by the CDC and Egyptian authorities revealed that a great amount of the exposure occurred during the 5 weeks she was in the US. This child's death, the first in the US in 10 years attributed to lead poisoning, reminds us that this environmental hazard continues to threaten children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



MEDBAG

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

Down 1. Speedball, 3. Rachael Carson, 6. Dextedrine, 7. OSHA, 10. HBO, 11. Antizol
 Across 1. Sarin, 2. Bufu, 4. TCA, 5. Dull, 6. Dilated, 8. HTN, 9. Theobromine

Answers: