New York State Poison Centers
1-800-222-1222

January 2006

The NY State Poison Centers

TOXICOLOGY LETTER

A Quarterly Publication • Vol. XI No. 1

Toxicology Advice Centers • •

Administrative Phone Numbers - To obtain a consult in your area, call 1.800.222.1222.

Western New York Poison Center (WNY)

716.878.7871 • http://wnypoison.org

Ruth A. Lawrence Poison and Drug Information Center Serving the Finger Lakes Region (FL)

585.273.4155 • www.FingerLakesPoison.org

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New York City Poison Control Center (NYC)

212.447.8152

Long Island Poison & Drug Info Center (LI)

516.663.4574 • www.LIRPDIC.org

Program Announcements • •

Ruth A. Lawrence: Monthly conference: every 4 weeks on Thursdays (11 am to noon), and every 4 weeks on Tuesdays (10 am-11 am).

UNY: Information on our Tenth Annual Toxicology Teaching Day to be coming!!

NYC: Consultants Case Conference • The first Thursday of the Month from 2-4pm

LI: Pre-Registration is required. Please contact Mr. Denis Jao at 516-663-2650 to register.

Both Telephone and Televideo broadcasts will be available.

Target Audience: Physicians, Pharmacists, Nurses, Physician-Assistants, Laboratory technicians, EMS staff, medical/nursing/pharmacy students and other healthcare professionals. CME Credits will be available for RN and MD's

Location: New Life Conference Rooms B&C
Winthrop-University Hospital
259 First Street
Mineola, Long Island, New York 11501

Times for ALL Conferences are: 12:15 PM-1:45 PM

Please call administrative telephone numbers for more information.

LI (cont'd):

Monday, January 23, 2006: TOXICITY, CONTRAINDICATIONS AND SAFETY OF HERBAL AND DIETARY SUPPLEMENTS

Elaine Yum, R. PH., CSPI, Director of HerbWatch
Long Island Regional Poison & Drug Information Center
Winthrop University Hospital, Mineola, NY

Monday, February 27,2006: UPDATE ON CANNABIS TOXICOLOGY

Michael McGuigan, MD, MBA, Clinical Professor of Emergency Medicine, SUNY/Stony Brook. Medical Director, Long Island Regional Poison Center at Medical Director, Winthrop University Hospital, Mineola, NY

Wednesday, March 22,2006: UPDATE ON THE TOXICOLOGY OF ANTIPSYCHOTICS AND ANTIDEPRESSANTS

Robin McFee, D.O., MPH, Clinical Assistant Professor, Preventive Medicine, SUNY/Stony Brook
Consultant Toxicology Educator, Long Island Regional Poison Center at Winthrop University Hospital,
Medical Director – Threat Science ™/Emergistics SM US

Monday, April 24,2006: Topic/Speaker: TBA

Wednesday, May 31,2006: Topic/Speaker: TBA

Wednesday, June 21,2006: Topic/Speaker: TBA

FDA Safety Summaries September-December 05

Methotrexate for Injection (preservative free)

FDA and Bedford Laboratories, a division of Ben Venue Laboratories, Inc., Bedford, Ohio, announced that it is voluntarily recalling one lot of Methotrexate for Injection (preservative free), USP 1 gram per vial (NDC 55390-143-01), Lot # 859142, exp 09/07, because the active drug substance ("ADS") used to manufacture Lot # 859142, contained low levels of ethylene glycol. *December 8, 2005*

Paroxetine HCl - Paxil and generic paroxetine

The FDA has determined that exposure to paroxetine in the first trimester of pregnancy may increase the risk for congenital malformations, particularly cardiac malformations. *December 8, 2005*

Aranesp (darbepoetin alfa)

Amgen and FDA notified healthcare professionals of revision to the WARNINGS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections of the prescribing information for Aranesp. The revised labeling provides updated safety information on reports of pure red cell aplasia and severe anemia, with or without other cytopenias, associated with neutralizing antibodies to erythropoietin in patients treated with Aranesp. *November 2005*

Epogen (epoetin alfa)
Procrit (epoetin alfa)

Amgen, Ortho Biotech and FDA notified healthcare professionals of revision to the WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections of the prescribing information for Epogen and Procrit. The revised labeling provides updated safety information on reports of pure red cell aplasia and severe anemia, with or without other cytopenias, associated with neutralizing antibodies to erythropoietin in patients treated with these products. *November 2005*

NovoSeven Coagulation Factor VIIa (Recombinant)

Novo Nordisk and FDA notified healthcare professionals of revisions to the WARNINGS and ADVERSE REACTIONS sections of the prescribing information for NovoSeven, to provide updated safety information on thrombotic and thromboembolic adverse events, based on clinical studies in non-hemophilia patients and on post-marketing safety surveillance. *November 23, 2005*

MBI Distributing, Inc. [Molecular Biologics] Over-The-Counter Eye Drops and Pain-Relieving Drugs

[Posted 11/30/2005] FDA notified consumers, caregivers, and healthcare professionals that MBI Distributing, Inc. (MBI), also known as Molecular Biologics, an over-the-counter [OTC] drug manufacturer of eye drops and other products will cease manufacturing and distributing drugs until it corrects manufacturing deficiencies and other violations. *November 29, 2005*

Flomax (tamsulosin HCl)

Boehringer Ingelheim and FDA notified healthcare professionals of revisions to PRECAUTIONS and ADVERSE REACTIONS sections of the prescribing information for Flomax, indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). A surgical condition termed Intraoperative Floppy Iris Syndrome (IFIS) has been observed during phacoemulsification cataract surgery in some patients treated with alpha-1 blockers including Flomax. *November 2005*

GenTeal Gel and GenTeal GelDrops

Novartis Ophthalmics and FDA notified healthcare professionals and patients of a voluntary recall due to a lack of sterility assurance of seven lots of two products. *November 16, 2005*

Long-acting Beta2-Adrenergic Agonists:

Advair Diskus (fluticasone propionate & salmeterol inhalation powder)
Foradil Aerolizer (formoterol fumarate inhalation powder)
Serevent Diskus (salmeterol xinafoate inhalation powder)

FDA notified manufacturers of Advair Diskus, Foradil Aerolizer, and Serevent Diskus to update their existing product labels with new warnings and a Medication Guide for patients to alert health care professionals and patients that these medicines may increase the chance of severe asthma episodes, and death when those episodes occur. *November 18, 2005*

Ortho Evra (norelgestromin/ethinyl estradiol transdermal system)

FDA notified healthcare professionals and patients of revisions to the label for Ortho Evra, a skin patch approved for birth control, that includes a bolded warning about higher exposure to estrogen

Continued on page 3

FDA Safety Summaries

Continued from page 2

for women using the weekly patch compared to taking a daily birth control pill containing 35 micrograms of estrogen. *November 10, 2005*

Amevive (alefacept)

Biogen Idec and FDA notified healthcare professionals of revisions to CONTRAINDICATIONS section of the prescribing information for Amevive, indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy. Amevive should not be administered to patients infected with HIV. Amevive reduces CD4+ T lymphocyte counts, which might accelerate disease progression or increase complications of disease in these patients. *October 2005*

Parenteral Maltose/Parenteral Galactose/ Oral Xylose-Containing Products

FDA notified physicians, nurses, medical technologists, pharmacists and other healthcare professionals of the potential for life-threatening falsely elevated glucose readings in patients who have received parenteral products containing maltose or galactose, or oral xylose, and are subsequently tested using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) based glucose monitoring systems. There have been reports of the inappropriate administration of insulin and consequent life-threatening/fatal hypoglycemia in response to erroneous test results obtained from patients receiving parenteral products containing maltose. *November 09, 2005*

Avinza (morphine sulfate extended-release capsules)

Ligand Pharmaceuticals Inc. and FDA notified healthcare professionals of revisions to BOXED WARNING, WARNINGS, PRECAUTIONS, CLINICAL PHARMACOLOGY, and DOSAGE AND ADMINISTRATION sections of the prescribing information to highlight and strengthen the warning that patients should not consume alcohol while taking Avinza. *October 2005*

Zevalin (ibritumomab tiuxetan)

] Biogen Idec and FDA notified healthcare professionals of revision to BOXED WARNINGS, WARNINGS, and ADVERSE REACTIONS sections of the Prescribing Information to describe severe cutaneous or mucocutaneous reactions, some with fatal outcome, that have been reported in association with the Zevalin therapeutic regimen in the post-marketing experience. *October 2005*

Cylert and generic pemoline products

FDA has concluded that the overall risk of liver toxicity from Cylert and generic pemoline products outweighs the benefits of this drug. In May 2005, Abbott chose to stop sales and marketing of Cylert in the U.S. All generic companies have also agreed to stop sales and marketing of this product. *October 24, 2005*

Cymbalta (duloxetine hydrochloride)

Eli Lilly and FDA notified healthcare professionals of revision to the PRECAUTIONS/Hepatotoxicity section of the prescribing information for Cymbalta (duloxetine hydrochloride), indicated for treatment of major depressive disorder and diabetic peripheral neuropathic pain. Postmarketing reports of hepatic injury (including hepatitis and cholestatic jaundice) suggest that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. *October 05, 2005*

Strattera (atomoxetine)

The FDA directed Eli Lilly and Company (Lilly), the manufacturer of Strattera (atomoxetine), to revise the prescribing information to include a boxed warning and additional warning statements that alert health care providers of an increased risk of suicidal thinking in children and adolescents being treated with this medication. *September 29, 2005*

Fluorouracil Injection 50mg/mL, (500 mg/10mL Single Dose Vial)

American Pharmaceutical Partners, Inc. and FDA notified healthcare professionals about a nationwide recall of Fluorouracil Injection 50 mg/mL (500 mg/10ml Single Dose Vial) because of the potential for invisible glass particles containing silica and aluminum in vials of the product. *September 2005*

Toprol-XL (metoprolol succinate) extended release tablets

Topamax (topiramate) tablets

Tegretol (carbamazepine)

Tegretol-XR (carbamazepine extended-release)

AstraZeneca and FDA notified healthcare professionals reports of medication dispensing or prescribing errors between Toprol-XL (metoprolol succinate) extended release tablets, indicated for the treatment of hypertension, long-term treatment of angina pectoris, and heart failure NYHA Class II or III, and Topamax (topiramate), a product of Ortho-McNeil Neurologics, Inc, indicated for the treatment of epilepsy and migraine prophylaxis. *October 2005*

Symptomatic Hypoglycemia

Case Report:

Contributed by: Liza Halcomb, M.D., Fellow in Medical Toxicology, NYCPCC

A six-year-old girl was noted to be sleeping in class, but was unarousable when the teacher tried to wake her. EMS was called and when the paramedics arrived, they documented a blood glucose of 20 mg/dL by fingerstick. The child was given intravenous glucose (as D50W), with improvement, and taken to the hospital. In the ambulance, she was given candy and drank a soda.

When she arrived to the hospital, she was awake and alert. Her vital signs were: BP, 121/63 mmHg; pulse, 120 beats/min; respiratory rate, 22 breaths/min; and temperature, 36.6C. In the ED, the patient's glucose was 42 mg/dL, she was asymptomatic and her exam was otherwise normal.

What are the initial steps to take in the care of this patient?

This patient had symptomatic hypoglycemia with a critically low blood sugar. It is essential to raise the serum glucose concentrations of these patients rapidly to prevent prolonged neuroglycopenia, which may lead to permanent brain injury. This child received intravenous glucose by the paramedics and she promptly woke up. In adults D50W (0.5 to 1 gm/kg) is typically administered, whereas small children should be given D25W because it is less irritating to the patient's veins. D50W contains 50% dextrose in water, or 50 grams dextrose/100 mL, and is packaged in 50 mL vials containing 25 grams of dextrose. The other important step in evaluating this patient is to assess why she became hypoglycemic.

What other pharmacological agents used to treat symptomatic hypoglycemia?

If the patient is unconscious and access is an issue, glucagon can be administered intramuscularly at a dose of 0.5 mg in patients under 44 pounds and 1 mg in patients who are over 44 pounds. Although this is generally effective, it relies on the enhanced breakdown of glycogen and will be ineffective if the patient's glycogen stores are depleted.

After waking up, the patient should be fed, instead of being put on a dextrose infusion. Food has many more calories than can be realistically administered intravenously. For example, a D10W infusion, typically recommended for patients with sulfonylurea-induced hypoglycemia, contains 10 grams of dextrose per 100 mL. Thus, a patient placed on 100 mL per hour will be getting 40 calories per hour of dextrose (4 calories/gram dextrose), compared to several hundred calories obtained by eating a sandwich. Furthermore, the kinetics of absorption of oral glucose are more favorable (once normoglycemia has been reestablished) than intravenous glucose and do not lead to dramatic swings in a patient's serum glucose concentration. This is important to prevent glucose-induced insulin release.

In many patients with sulfonylurea-induced hypoglycemia, once a patient has become symptomatic, octreotide is often indicated. Sulfonylureas "sensitize" glucose-triggered insulin release by the Islet cells of the pancreas. The role of octreotide is to prevent enhanced insulin release from the pancreatic Islet cells in response to normal or elevated serum glucose concentrations. This is a particularly important phenomenon in patients who receive intravenous concentrated glucose (e.g., D50W, D25W) because the extreme rise in the blood concentration of glucose (to several hundred mg/dL) may trigger the massive release of insulin, leading to profound rebound hypoglycemia an hour or so later.[1] Octreotide prevents hyperinsulinemia by binding to a receptor that prevents the influx of calcium into the pancreatic islet cells.[2] In adults the dose is 50 mcg subcutaneously every six hours and in children it should be 1-1.5 mcg/kg every six hours. It is common to continue the octreotide for 24 hours and then observe the patient for 24 hours following discontinuation of the octreotide.

Are there any concerns in treating sulfonylurea induced hypoglycemia?

As noted, in the presence of sulfonylureas repeat boluses of dextrose stimulate the pancreas to release insulin, which can result in rebound hypoglycemia. Therefore, it is important to feed the patient in order to avoid fluctuating glucose levels.

Case Continuation

The patient stated that approximately 48 hours prior to presentation she had eaten one of her grandmother's glipizide pills because she was told it was a "sugar pill". The next day she was slightly more fatigued than usual, but was not symptomatic enough to require medical attention.

Continued on page 5

Symptomatic Hypoglycemia

Continued from page 4

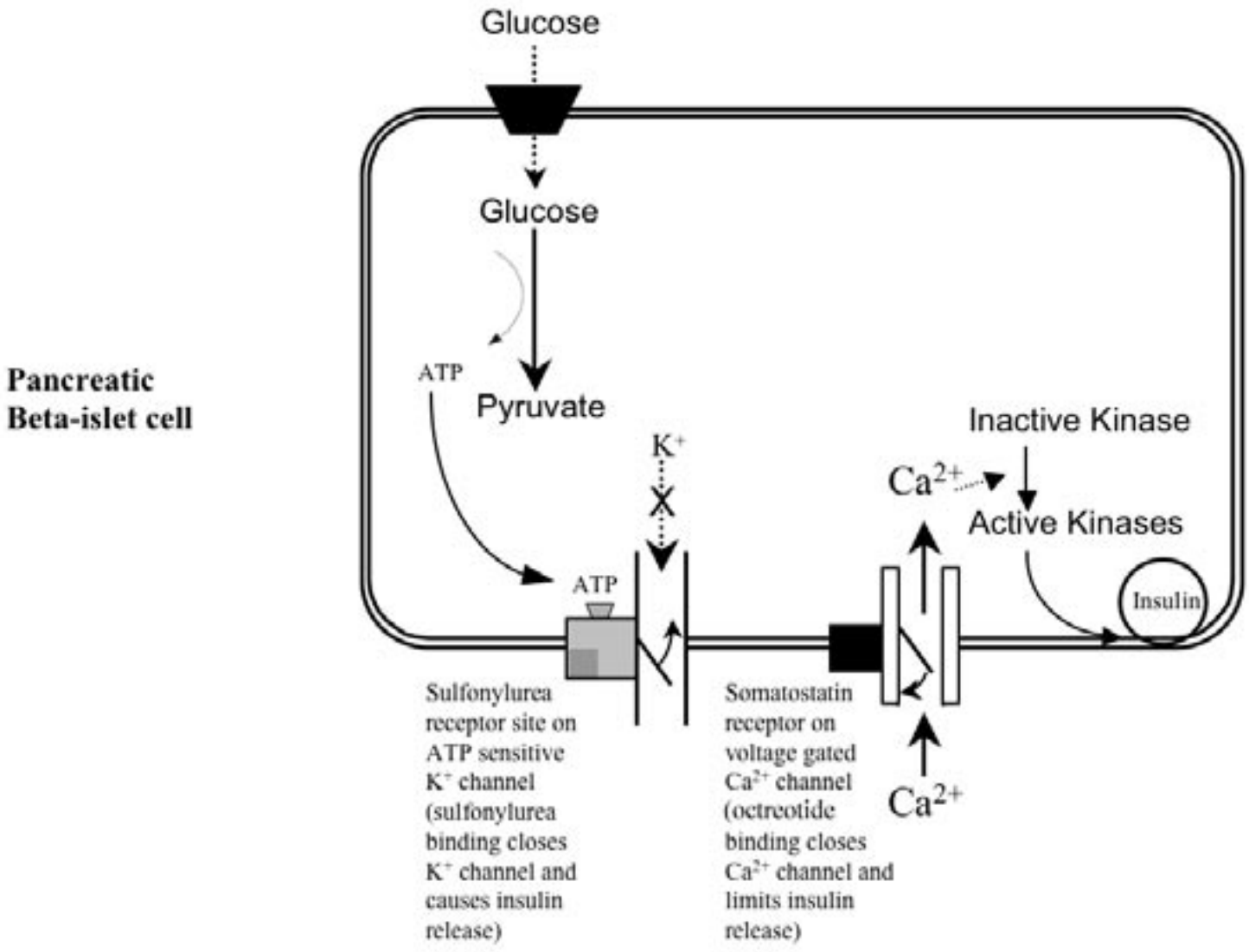
After she was fed, she was transferred to another hospital where 25 mcg of octreotide was administered subcutaneously every 6 hours for 24 hours.

Her laboratory results drawn on presentation were as follows: Proinsulin: 366.0 pmol/L (range: 2.1-26.8), Insulin: 112 mcIU/mL (range: 0.0-15.6), C-Peptide: 8.8 ng/mL (range: 1.1-4.6), Glipizide: 1 ng/mL (therapeutic: 100-1000 ng/mL). These values are consistent with glipizide ingestion because they confirm high levels of endogenous insulin in the setting of profound hypoglycemia. In addition the low (but present) serum level of glipizide confirms ingestion and suggests that she had taken the drug many hours prior to her hypoglycemic event.

Although chlorpropamide may produce hypoglycemia that begins up to 48 hours after ingestion, the delay with other sulfonylureas is generally shorter. A recent prospective study suggested that an eight-hour observation time in the ED is sufficient to exclude toxicity associated with sulfonylurea ingestions.[3] However, most patients in these studies had unconfirmed exposures. This case illustrates that life-threatening hypoglycemia can begin long after the suggested 8-hour observation period, and may be delayed by as much as 48 hours and reinforces the previously held belief that all children with sulfonylurea ingestions should be admitted to the hospital.

References:

1. *Boyle PJ, et al. Octreotide reverses hyperinsulinemia and prevents hypoglycemia induced by sulfonylurea overdoses. J Clin Endocrin Metab 1993; 76(3): 752-756.*
2. *Carr R, Zed PJ. Octreotide for sulfonylurea-induced hypoglycemia following overdose. Ann Pharmacother 2002;36:1727-1732.*
3. *Spiller HA et al. Prospective multicenter study of sulfonylurea in children. J Pediatr. 1997;131:141-146.*



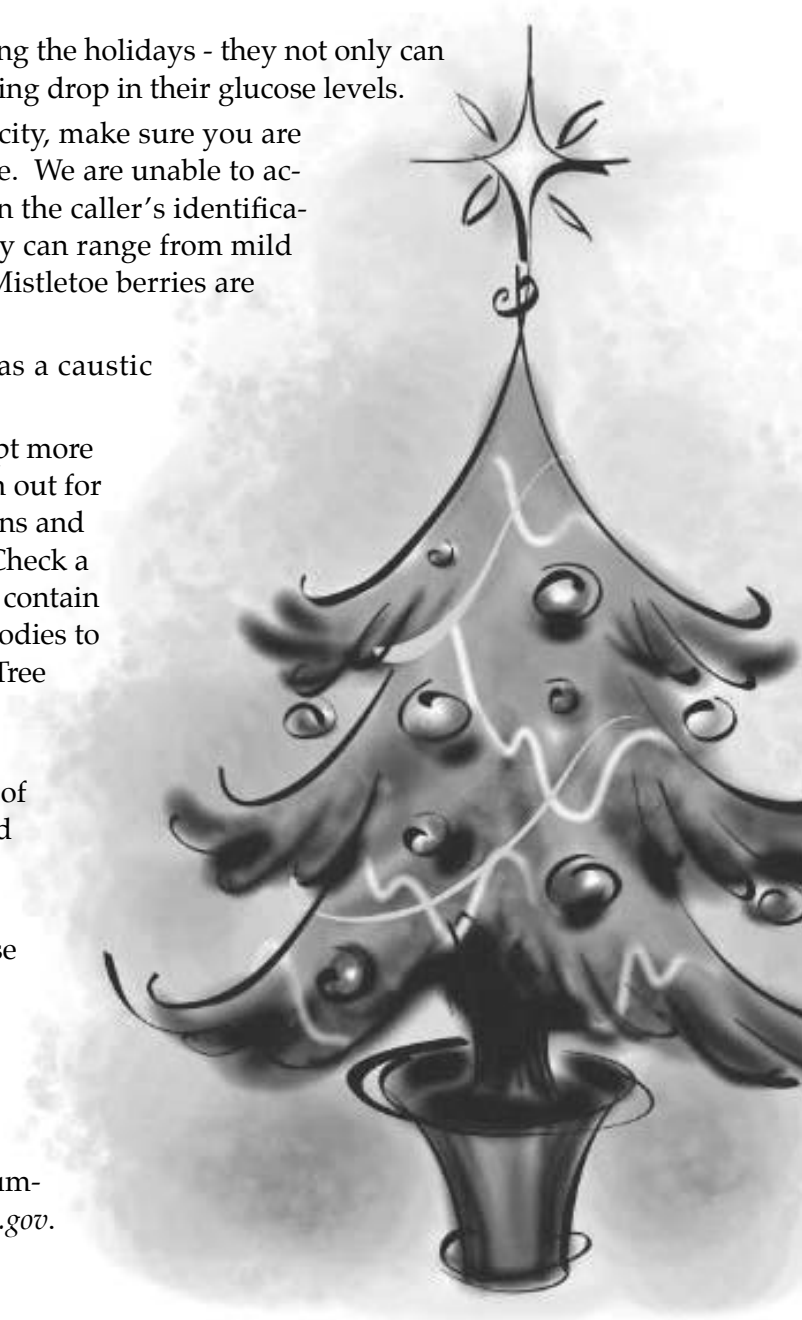
Adapted from Goldfranks Toxicologic Emergencies, 7th Edition

SPI CORNER TOPIC:
WINTER HOLIDAY TOXINS

Contributed by: Deborah Anguish, RN, CSPI, Upstate New York Poison Center, Syracuse, NY.

Did your family receive some potentially toxic gifts? Remember some gifts should be used with caution. In addition to tiny pieces or stringed objects causing choking, many products contain toxic substances. Below is a list of items of particular concern:

- **Art products** - Remember to supervise young children as some crayons contain lead and could be harmful if swallowed.
- **Play toys:**
  - Water yo-yo balls can contain kerosene and may harm children if ingested.
  - Chemistry sets contain material that can be harmful to children, do not assume since they are made for children they contain non toxic substances or materials.
- **Household products**
  - Alcoholic beverages that tend to be left out during the holidays - they not only can get intoxicated, children can have a life threatening drop in their glucose levels.
  - Plants - Many house hold plants can cause toxicity, make sure you are familiar with the species of plants in your home. We are unable to accurately identify plant on the phone and rely on the caller's identification to determine potential for Toxicity. Toxicity can range from mild irritation, to kidney/liver damage. Holly and Mistletoe berries are also toxic.
  - Batteries can cause a choking hazard as well as a caustic injury hazard.
  - CO - Increasing home heating prices may prompt more indoor inappropriate use of space heaters-Watch out for an increase in Carbon Monoxide exposures. Signs and symptoms range from flu like to coma/death. Check a CO level to be sure. Furniture strippers can also contain methylene chloride; which is converted in our bodies to Carbon Monoxide, causing toxicity. Christmas Tree Bubble lights contain methylene chloride.
  - Antifreeze products are highly toxic in small amount to humans and animals, one sip (5 cc's) of 100% methanol or ethylene glycol in a 10kg child would be toxic and most likely will require the antidote Fomepizole or even Hemodialysis.
  - Medications - Hectic holiday schedules can cause us all to alter our usual rituals, we can forget to take our medications on time or take too much. We can forget and leave medications out where children may find and take them. Exercise caution with all medications.

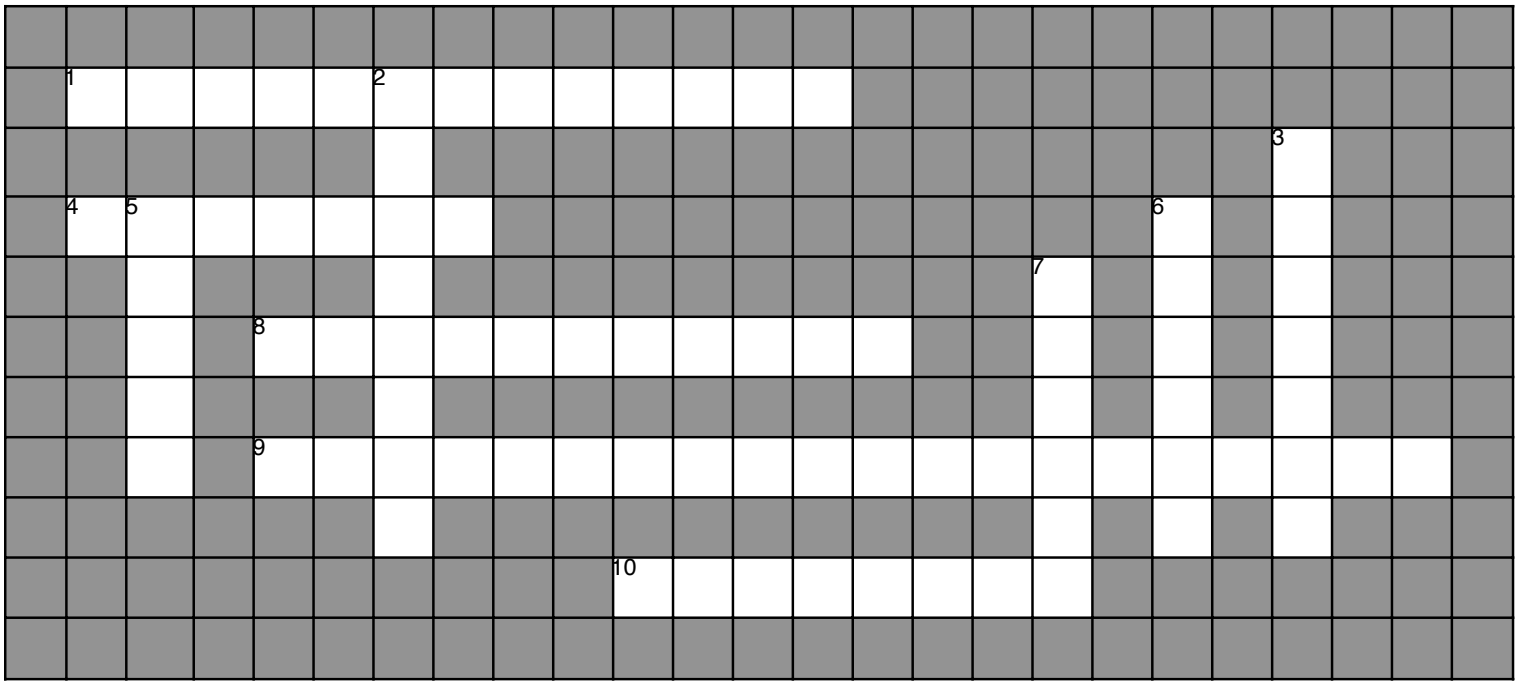


You can check specific products by contacting the Consumer Products Safety Commission product recalls at *www.cpsc.gov*.

TOXICOLOGY CROSSWORD

CCB TOXICITY

Contributed by: Mary Halsey-Claps, RN, CSPI, Upstate New York Poison Control Center, Syracuse, NY



Across

1. What is the typical finding on serum chemistry testing of CCB?
4. Avoid administration of X if cardiac glycoside toxicity may be present.
8. In addition to hypotension, what vital sign abnormality is classic for CCB overdose?
9. Overdose of ccb-sustained release preparations require what type of gut decontamination?
10. Extracorporeal method of not value in managing overdose of CCB.

Down

2. May be administered early for presence of bradycardia or hypotension especially if a concurrent beta-blocker is suspected.
3. Is a new therapy for bradycardia and hypotension.
5. Overdose patient may be X even though they may be bradycardiac and hypotensive
6. Which decontamination agent should be avoided in an overdose of a ccb due to its possible vagal effects?
7. Is the first line therapy for hypotension.

Answers: Crossword: Across: 1. Hyperglycemia; 4. Calcium; 8. Bradycardia; 9. Whole bowel irrigation; 10. Dialysis; Down: 2. Glucagon; 3. Insulin; 5. Alert; 6. Ipecac; 7. Fluids

State University of New York
Upstate Medical University

Upstate NY Poison Center
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Monday, March 27, 2006: UPDATE ON THE AVIAN FLU

Robin McFee, D.O., MPH
Clinical Assistant Professor, Preventive Medicine, SUNY/Stony Brook
Consultant Toxicology Educator, Long Island Regional Poison & Drug Information Center at Winthrop University Hospital

Monday, April 24, 2006:MARINE TOXICOLOGY

Jessica A. Fulton, D.O.
Fellow, NY City Poison Center
New York University and Bellevue Hospital Center
New York, NY

Wednesday, May 31, 2006: UPDATE OF PEDIATRIC TOXICOLOGY

Kevin Osterhoudt, MD, MSCE, FAAP, FAMCT
Medical Director, The Poison Center at the Children's Hospital of Philadelphia
Philadelphia, PA

Wednesday, June 21, 2006: TBA

Speaker: TBA

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Update from the Educator: *Nancy Warburton, RN, BSN*

The Educators of the New York State Poison Centers are collaborating with SUNY Albany School of Public Health to develop two satellite telecommunication programs which will be broadcast statewide to provide poison prevention information to the public.

The first program will air on April 27, 2006 The one hour presentation will be followed by a question and answer session. This program is designed for community service professionals such as Public Health Nurses, childcare workers and program administrators. The second program, which will air in the fall, will be developed for children.

The programs are funded by a grant from the Department of Health and Human Services Health Resources and Services Administration (HRSA). Dr. Ruth Lawrence is the Principal Investigator. The free programs will be broadcast via satellite to any organization with downlink capability. Nursing Contact Hours, CME, and CHES credits are available for participation in this program.

Interested participants may register by calling 518-402-0330 or on the web at *http://tinyurl.com/7ge4u*.

Please call administrative telephone numbers for more information.

Tracleer (bosentan)

Actelion and FDA notified healthcare professionals of changes to the prescribing information based on cases of hepatotoxity reported. *March 01, 2006*

Cefazolin for Injection

Hanford Pharmaceuticals and FDA notified healthcare professionals about the recall of four lots (379,975 vials) of Cefazolin for Injection, USP, 1 g/10 mL vials, an antibiotic used in a hospital environment to treat skin and skin structure, respiratory and other infections. Certain lots of the active ingredient used to manufacture the product have been shown to contain microbial contamination (Bacillus pumilus, Staphylococcus hominis, Propionibacterium acnes, or Micrococcus luteus) which may pose a serious or life-threatening risk for some patients. *February 2006*

Tequin (gatifloxacin)

BMS notified FDA and healthcare professionals about proposed changes to the prescribing information for Tequin, including an updating of the existing WARNING on hypoglycemia (low blood sugar) and hyperglycemia (high blood sugar), and a CONTRAINDICATION for use in diabetic patients. *February 15, 2006*

Nimotop (nimodipine)

Bayer and FDA notified healthcare professionals of changes to the prescribing information for nimodipine (Nimotop), including a boxed warning to notify prescribers about medication administration errors with nimodipine.

Benzocaine sprays

FDA issued a Public Health Advisory to notify healthcare professionals and patients about adverse events, including methemoglobinemia, associated with the use of benzocaine sprays used in the mouth and throat. *February 10, 2006*

Trasylol (aprotinin)

FDA issued a public health advisory and other advisory information to notify both healthcare professionals and consumers of recently published studies of serious renal and cardiovascular toxicity following Trasylol administration to patients undergoing coronary artery bypass grafting surgery (CABG). *February 08, 2006*

Hydrea (hydroxyurea capsules)

Droxia (hydroxyurea capsules)

Bristol-Myers Squibb notified healthcare professionals about revisions to the WARNINGS and ADVERSE REACTIONS sections of the prescribing information to describe cutaneous vasculitic toxicities, including vasculitic ulcerations and gangrene, in patients with myeloproliferative disorders during therapy with hydroxyurea, most often reported in patients with a history of or currently receiving interferon therapy. *January 20, 2006*

Ketek (telithromycin)

Annals of Internal Medicine published an article reporting three patients who experienced serious liver toxicity following administration of Ketek (telithromycin). *January 20, 2006*

Elidel Cream (pimecrolimus)

Protopic Ointment (tacrolimus)

The Food and Drug Administration announced the approval of updated labeling for two topical eczema drugs, Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus). The labeling will be updated with a boxed warning about a possible risk of cancer and a Medication Guide (FDA-approved patient labeling) will be distributed to help ensure that patients using these prescription medicines are aware of this concern. *January 19, 2006*

Brazilian Diet Pills (Emagrece Sim and Herbathin products)

The FDA warned consumers not to use two unapproved drug products that are being marketed as dietary supplements for weight loss. Emagrece Sim Dietary Supplement, also known as the Brazilian Diet Pill, and Herbathin Dietary Supplement may contain several active ingredients, including controlled substances, found in prescription drugs that could lead to serious side effects or injury. They contain chlordiazepoxide HCl (the active ingredient in Librium), and fluoxetine HCl (the active ingredient in Prozac). Emagrece Sim and Herbathin were also found to contain Fenproporex, a stimulant that is not approved for marketing in the United States. *January 13, 2006*

Continued on page 3

FDA Safety Summaries

Continued from page 2

Clozaril (clozapine) tablets

Novartis and FDA notified healthcare professionals of revisions to the BOXED WARNING, WARNINGS, CONTRAINDICATIONS, PRECAUTIONS (Information for Patients and Pharmacokinetic-Related Interactions subsections), and ADVERSE REACTIONS (Postmarketing Clinical Experience subsection) sections of the prescribing information for Clozaril (clozapine) tablets. Recommendations from the FDA's Psychopharmacological Drugs Advisory Committee regarding the white blood cell monitoring schedule, required for all clozapine users, has resulted in modification in the monitoring schedule. *December, 2005*

Avandia (rosiglitazone maleate)

Avandamet (rosiglitazone maleate/ metformin HCl)

GlaxoSmithKline and FDA notified healthcare professionals about post-marketing reports of new onset and worsening diabetic macular edema for patients receiving rosiglitazone. *December 2005*

Fraudulent Avian Flu Therapies

FDA notified healthcare professionals and patients that it issued warning letters to nine companies marketing bogus flu products behind claims that their products could be effective against preventing the avian flu or other forms of influenza. *December 13, 2005*

Flowers, Bulbs and Toxins

Case Report:

Contributed by: Ruth A. Lawrence, MD, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY

No matter how long the winter or how deep the snow, everyone looks forward to spring and the flowers, bushes and trees that come to life. With the blossoms, however, comes the hazard of those plants, bulbs, berries and fruits that are toxic.

Early in the season, impatient gardeners start with a few bulbs, some pebbles and a dish of water. Voila! Flowers appear while presenting a ready-to-eat temptation easily accessed by the infant or toddler. Calls to the poison center about spring bulbs are numerous.

Narcissus

The Liliaceae family includes many species of lily including the edible onion, garlic and chives but also includes some that are very toxic.

The most common bulbs are narcissus, amaryllis, daffodils, jonquils and tulips. Adults and curious toddlers have mistakenly eaten their onion-like bulbs. These bulbs are often left in the garage, planted in water on the table or the flowers picked for display in a vase, all tempting and easily accessed.

Onion "Bulbs"

The Amaryllis species also cause dermatitis in some individuals especially gardeners and florists who handle them frequently. Cattle and rabbits may develop symptoms of respiratory failure when they eat these bulbs while squirrels seem to relish them. A sample but not an exhaustive list appears in the accompanying table.

Flower Bulbs

Liliaceae Family

Narcissus Species

Amaryllidaceae

Daffodil, jonquil, Narcissus, Paciencia

- all parts are toxic
- ingestion of the bulbs – mistaken for onions
- toxin: lycorine and related alkaloids
- symptoms – nausea, vomiting (often persistent), diarrhea and shivering
- management – fluid replacement

Daffodil

Flowers, Bulbs and Toxins

Continued from page 4

Hyacinthus Species (hyancinth) – intense stomach cramps, vomiting and diarrhea. Treatment includes fluids and supportive care


Hyacinth

Tulipe Species (tulip) – similar symptoms and treatment as above


Tulip

Lily Species – all members are toxic in all their parts especially the bulb.

Gloriosa superba (Glory lily) – characteristic upside down flowers. All parts are poisonous especially the tubers. Contains alkaloids that are extremely poisonous, which produces numbness of lips, tongue, and throat, abdominal pain and burning, vomiting and diarrhea and in severe cases difficulty breathing, convulsions and death. Treatment is supportive and symptomatic.


Glory Lily

Lily of the Valley – leaves, flowers, roots and especially fruits (red berry) are all toxic. Contains cardiac glycosides (convallarin and convaillamarin) with a digitalis-like effect causing irregular heartbeat with EKG changes and gastrointestinal symptoms (n, v, d). Of the ten plant exposures that contain cardioglycosides, five of the cases involved Lily of the Valley at our center in 2005. Treatment is supportive and may include potassium, procainamide, quinidine sulfate or disodium salt of edetate (Na2EDTA). Can produce coma and death.


Lily of the Valley

SPI CORNER:

SPRING CLEANING

Contributed By: Norma Barton, RPh, CSPI, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY

When the snow melts and temperatures start warming up, thoughts turn to the ritual of Spring cleaning. Usually the first task is assembling the cleaning supplies that include brand name items such as Lysol, Formula 409, Mr. Clean, and Windex, along with store brands and bleach and ammonia. There is a feeling by some that more is better and using more than one product at a time will increase the cleaning power. But adding one cleaning product to another such as adding bleach and ammonia together can cause a chemical reaction and formation of a gas that can be very irritating to the eyes, throat and upper respiratory tract. Transient shortness of breath, cough, watery eyes can result. This may precipitate an asthma attack for susceptible individuals. For the former individuals, getting fresh air and sipping on liquids will help to ease the symptoms. But for the latter, a trip to the emergency department may be necessary.

Often, cleaning involves being in a closed or small area such as a bathroom. Bleach and bowl cleaner or drain cleaner can release chlorine gas which is an emergency. Spraying or applying a large quantity of cleaning solution will fill the room quickly with fumes. These fumes and odors can be very annoying and irritating. So remember to ventilate each area well so that there is not a build-up of odor and fumes and use small amounts to cover small areas rather than entire surface.

Remember also that cleaning solutions are irritating to the skin, so wearing protective gloves will protect the skin from these harsh chemicals.

For some, the late Spring means opening the pool. When opening the container of pool chemicals, usually chlorine or bromine, make sure the lid is removed slowly so any build-up of gas can be vented slowly. This should all be done outside keeping the container at arm's length. Vapors given off by these chemicals are very irritating. This procedure also applies to the place in the pool where the chemicals are added.

Of course, above all, make sure that household cleaning supplies and chemicals are stored properly and in a secure cabinet unreachable by children and pets.

GENERAL DANGERS FROM GARDENING CHEMICALS

Contributed By: Sharon Benware, RN, CSPI, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY

Many products are available to minimize weeds and pests in the garden. Some products are potentially toxic depending on formulation and exposure route.

Herbicides (such as Round Up) contain glyphoshates and surfactants. The presence of surfactants is believed to be responsible for the majority of adverse reactions. Skin exposure can cause mild to severe irritation. Conjunctivitis can occur with splash contact to eyes. Inhalation of fumes can cause respiratory irritation. Ingestion can cause mouth and/or throat irritation, vomiting or diarrhea.

In the event of skin contact, thorough washing is recommended. For eye contact, flush with water for several minutes. If redness remains, an eye exam by an ophthalmologist is recommended. If inhaled, fresh air and rest are recommended. If cough persists, medical evaluation is recommended. For inadvertent ingestion, rinse the mouth and drink up to a glass of water or milk as long as breathing is not affected.

Organophosphates are present in some commercially available pesticides, and can still be found in discontinued products for home use. These products require special handling, clean up and disposal. Muscarinic, nicotinic and central effects are possible following inhalation, skin exposure, or ingestion. Multiple washings are recommended following skin exposure, with removal and possible disposal of contaminated clothing. Specialized assessment and treatment is recommended following acute poisoning, including determination of plasma and red blood cell cholinesterase activities. Atropine is indicated for treatment of muscarinic effects (such as tearing, salivation, and bradycardia) and Pralidoxime for nicotinic effects (muscle weakness or paralysis and CNS effects).

Slug baits may contain metaldehyde, a strong irritant. It should never be applied to edible portions of plants. Toxicity is possible following ingestion, skin contact, or inhalation of fumes. Ingestion can cause symptoms ranging from mouth irritation or nausea and vomiting, kidney or liver damage, and central or respiratory effects. Skin or eye contact can cause minor to severe irritation.

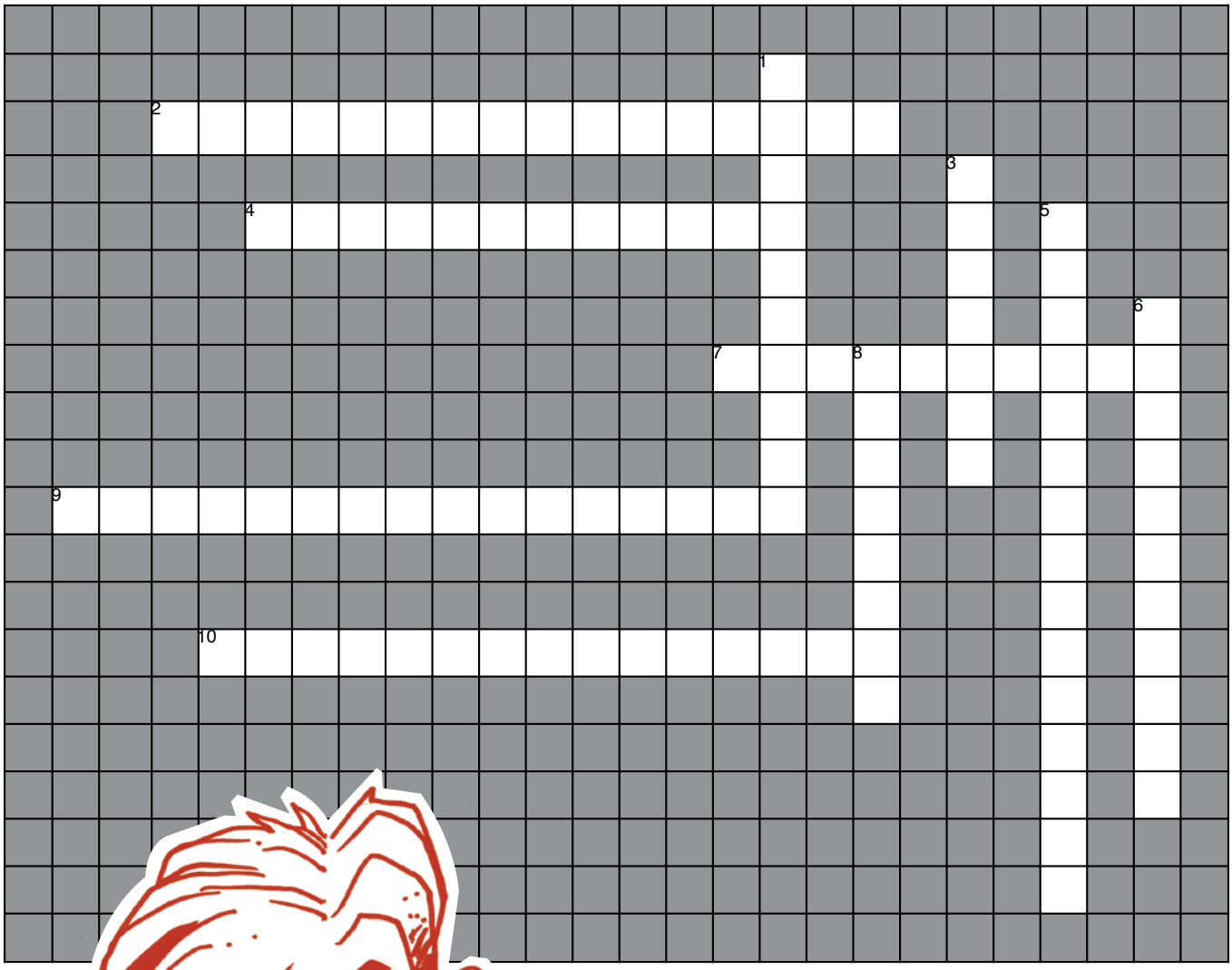
Many alternatives to gardening chemicals are available, including natural products and selection of plants which are most resistant to diseases and pests such as marigolds to repel squirrels and rabbits.

Continued on page 8

TOXICOLOGY CROSSWORD

SPRINGTIME HOUSEHOLD HAZARDS

Contributed by: Mary Halsey-Claps, RN, CSPI, Upstate New York Poison Control Center, Syracuse, NY



Across

2. Corrosive/acid ingredient in rust removers
4. Irritant ingredient found in bleach
7. Potentially toxic ingredient in many herbicides
9. Eye irritant found in glass cleaners
10. Corrosive/base found in oven cleaners

Down

1. Irritant ingredient in some furniture polish
3. Irritant found in some floor cleaners
5. Potentially toxic ingredient in some insecticides
6. Potentially toxic substance in slug bait
8. Irritant found in air fresheners

Answers: Across: 2. Hydrogenfluoride; 4. Hypochlorite; 7. Glyphosate; 9. Isopropylalcohol; 10. Sodiumhydroxide. **Down**: 1. Mineral oil; 3. Pineoil; 5. Organophosphate; 6. Metaldehyde; 8. Perfumes.

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Table of Springtime Household Hazards

Contributed by: Cindy Bichler, BSN, CSPI, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY

Indoor Products

Irritants	Ingredients
Bleach	Hypochlorite
Glass cleaners (with eye exposure)	Isopropyl Alcohol
Floor cleaners (Pinesol, Mr. Clean)	Pine oil, detergents
Air fresheners (plug ins, sprays)	Propellants, perfume
Risk of Aspiration	
Furniture polish (Pledge, Old English)	Mineral oil
Mineral spirits	
Corrosive/Acids	
Oven Cleaners (Easy-Off)	Sodium Hydroxide
Rust removers	Hydrofluoric acid
Mold and Mildew Removers (Tilex)	Sodium Hydroxide

Outdoor Products

Irritants	
Fertilizers (with larger ingestions)	
Risk of Aspiration	
Gasoline	
Lighter fluid	
Potentially toxic	
Herbicides (Round Up)	Glyphosate
Insecticides (Daycon)	Organophosphate
Slug Bait	Metaldehyde

State University of New York
Upstate Medical University
Upstate NY Poison Center
750 East Adams Street
Syracuse, NY
13210

New York State Poison Centers
1-800-222-1222

August 2006

The NY State Poison Centers

TOXICOLOGY LETTER

A Quarterly Publication • Vol. XI No. 3

Program Announcements • •

Ruth A. Lawrence: Monthly conference: every 4 weeks on Thursdays (11 am to noon), and every 4 weeks on Tuesdays (10 am-11 am).

CNY: Please mark your calendars for our Tenth Annual Toxicology Teaching Day on November 15, 2006. More information to follow!!!

NYC: Consultants Case Conference • The first Thursday of the Month from 2-4pm

LI: Pre-Registration is required. Please contact Mr. Denis Jao at 516-663-2650 to register.

Both Telephone and Televideo broadcasts will be available.

Target Audience: Physicians, Pharmacists, Nurses, Physician-Assistants, Laboratory technicians, EMS staff, medical/nursing/pharmacy students and other healthcare professionals.

Location: New Life Conference Rooms B&C
Winthrop-University Hospital
259 First Street
Mineola, Long Island, New York 11501

Times for ALL Conferences are: 12:15 PM-1:45 PM

Wednesday, June 21, 2006: UPDATE ON THE TOXICOLOGY OF NEW ANTIPSYCHOTICS AND ANTIDEPRESSANTS

Speaker: Robin McFee, D.O., MPH, Clinical Assistant Professor, Preventive Medicine, SUNY/Stony Brook Consultant Toxicology Educator, Long Island Regional Poison Center at Winthrop University Hospital, Medical Director – Threat Science ™/Emergistics SM US

Other dates with topic and speaker TBD:

Tuesday, September 25, 2006
Tuesday, October 31, 2006
Wednesday, November 29, 2006

The American Academy of Clinical Toxicology announced the formation of a Special Interest Group (SPI G) in Herbs & Dietary Supplements in October 2005. For more information, contact the co-chairs Alan Woolf (*alan.woolf@childrens.harvard.edu*) or Elaine Kang-Yum (*ekangyum@winthrop.org*)

Please call administrative telephone numbers for more information.

Tox Trivia • •

1. Slug bait contains this toxin.
2. Foxglove plants contain this toxin.
3. Malathion spraying can cause this toxidrome of symptoms.

NYPC Tidbits • •

1. What are "Wets"?
2. What is the target organ for toxicity from absinthe (not seeing a resurgence in use)?
3. What drug is associated with "Chasing the Dragon"?

Answers on page 3

Toxicology Advice Centers • •

Administrative Phone Numbers - To obtain a consult in your area, call 1.800.222.1222.

Western New York Poison Center (WNY)
716.878.7871 • http://wnypoison.org

Ruth A. Lawrence Poison and Drug Information Center Serving the Finger Lakes Region (FL)
585.273.4155 • www.FingerLakesPoison.org

Upstate New York Poison Center (UNY)
315.464.7078 • www.cnypoison.org

New York City Poison Control Center (NYC)
212.447.8152

Long Island Poison & Drug Info Center (LI)
516.663.4574 • www.LIRPDIC.org

FDA Safety Summaries • March 2006 - June 2006

Gadolinium-containing Contrast Agents for Magnetic Resonance Imaging (MRI): Omniscan, OptiMARK, Magnevist, ProHance, and MultiHance

New reports have identified a possible link between NSF/NFD and exposure to gadolinium containing contrast agents used at high doses for a procedure called Magnetic Resonance Angiography (MRA). *June 8, 2006*

Angiotensin-converting enzyme inhibitor (ACE inhibitors) drug class

The New England Journal of Medicine published an article reporting that infants whose mothers had taken an angiotensin-converting enzyme inhibitor (ACE inhibitors) drug during the first trimester of pregnancy had an increased risk of major congenital malformations, compared with infants who had not undergone first trimester exposure to ACE inhibitor drugs. *June 6, 2006*

Tysabri (natalizumab)

FDA notified healthcare professionals of the resumed marketing, with a special restricted distribution program of Tysabri (natalizumab), a monoclonal antibody for the treatment of patients with relapsing forms of multiple sclerosis. Tysabri was initially approved by the FDA in November 2004, but was withdrawn by the manufacturer in February 2005 after three patients in the drug's clinical trials developed progressive multifocal leukoencephalopathy (PML). *June 05, 2006*

Tacrolimus Active Pharmaceutical Ingredient [API]

Spectrum Laboratory Products and FDA notified healthcare professionals of the recall of the active pharmaceutical ingredient tacrolimus, an immunosuppressive drug used to prevent rejections of transplanted solid organs such as heart or kidney, after learning that some lots of the ingredient are subpotent. *May 11, 2006*

Paxil (paroxetine hydrochloride) Tablets and Oral Suspension

Paxil CR (paroxetine hydrochloride) Controlled-Release Tablets GlaxoSmithKline (GSK) and FDA notified healthcare professionals of changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the prescribing Information for Paxil and Paxil CR. *May 2006*

Oral Sodium Phosphate (OSP) Products for Bowel Cleansing

FDA notified healthcare professionals and consumers of reports of acute phosphate nephropathy, a type of acute renal failure, that is a rare, but serious adverse event associated with the use of oral sodium phosphates (OSP) for bowel cleansing. *May 05, 2006*

Goldline Brand Extra Strength Genapap and Extra Strength Genebs (Acetaminophen 500 mg)

Recall of Goldline brand Extra Strength Genapap 500mg (Acetaminophen) Caplets and Tablets and Extra Strength Genebs 500mg (Acetaminophen) Caplets and Tablets due to a labeling error. *May 02, 2006*

NeutraGard 0.05% and NeutraGard Plus 0.2% Neutral Sodium Fluoride Anticavity Treatment Rinse

Pascal Company, Inc. recalled all lots and all flavors of NeutraGard 0.05% Neutral Sodium Fluoride Anticavity Treatment Rinse and NeutraGard Plus 0.2% Neutral Sodium Fluoride Anticavity Treatment Rinse packaged in clear 16 oz plastic bottles. The products were recalled because they may be contaminated with Burkholderia cepacia and Pseudomonas aeruginosa bacteria. *April 27, 2006*

Promethazine HCl (marketed as Phenergan and generic products)

FDA notified healthcare professionals and patients that cases of breathing problems, some causing death, have been reported to the FDA when the drug was used in children less than two years old. *April 25, 2006*

Continued on page 3

FDA Safety Summaries

Continued from page 2

Fungal Keratitis Infections Related to Contact Lens Use

On May 15, 2006, Bausch and Lomb announced its decision to permanently remove all ReNu with MoistureLoc products worldwide. As previously recommended, consumers should stop using ReNu with MoistureLoc immediately. *May 31, 2006*

Macugen (pegaptanib sodium injection)

(OSI)Eyetech/Pfizer and FDA notified healthcare professionals of important changes in the approved product labeling for Macugen (pegaptanib sodium injection), including changes to the CONTRAINDICATIONS, PRECAUTIONS, ADVERSE EVENTS Post-Marketing, and DOSAGE and ADMINISTRATION sections. Rare reports of anaphylaxis/anaphylactoid reactions, including angioedema following the administration of Macugen along with various medications administered as part of the injection preparation, were described. *March 6, 2006*

Diastat AcuDial (diazepam rectal gel)

Valeant Pharmaceuticals International and FDA notified healthcare professionals of complaints the company received concerning small cracks at the base of the plastic tip of the applicators with resulting leakage of the medication when the plunger is depressed, preventing full dosing and potentially resulting in a sub-optimal therapeutic response. *March 30, 2006*

Mifeprex (mifepristone)

FDA notified healthcare professionals of two additional deaths following medical abortion with mifepristone (Mifeprex). *March 17, 2006*

Ontak (denileukin diftitox)

Ligand Pharmaceuticals and FDA notified healthcare professionals of changes to the WARNINGS section of the prescribing information for Ontak, indicated for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma. Loss of visual acuity, usually with loss of color vision, has been reported following administration of Ontak. *March 03, 2006*

Illegal Steroid Products Sold as Dietary Supplements

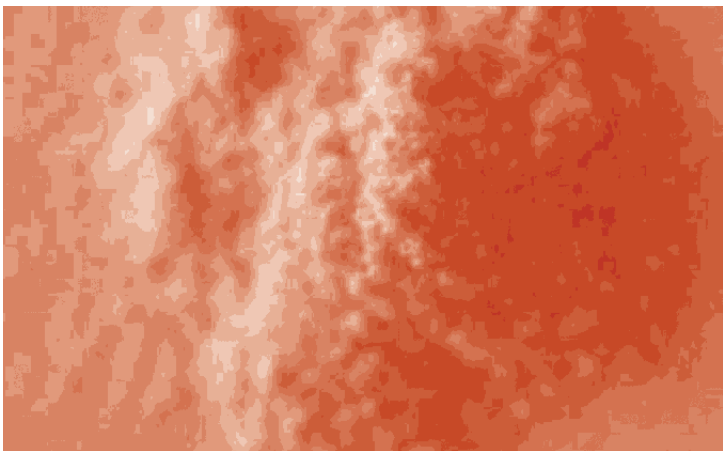
The FDA warned several manufacturers and distributors of unapproved drugs containing steroids that are marketed as dietary supplements and promoted for building muscle and increasing strength that the products may cause serious long-term adverse health consequences in men, women, and children. *March 09, 2006*

Tox Trivia ANSWERS • •

1. metaldehyde
2. digitalis glycosides
3. Cholinergic

NYPC Tidbits ANSWERS • •

1. Cigarettes (Tobacco or marijuana) dipped in a liquid (usually embalming fuid or formaldehyde) which is laced with phencyclidine (PCP)
2. CNS neurotoxicity
3. Heroin



A Fatal Ingestion
Case Report:

Contributed by: Ka Wing (Carmen) Lee, PharmD. Candidate. St. John's University, T Caraccio, Pharm.D., ABAT, J Flori, RN, CSPI, J Leonard, RN CSPI, Long Island Regional Poison and Drug Information Center at Winthrop University Hospital, Mineola, NY

An 83-year-old male presented to the emergency department via ambulance after ingesting unknown amounts of verapamil (both immediate release and sustained release preparations), sertraline, trazodone, lorazepam, lisinopril, hydrochlorothiazide, and finasteride at an unknown time. He was last seen awake and alert approximately 4 hours previous. In the emergency department, the patient appeared lethargic and weak with a heart rate of 60 beats per minute, blood pressure of 54/30 mmHg and was afebrile. His past medical history was unknown and neither his family, physician nor other health care providers could be reached.

What are the appropriate initial measures for this patient?

Appropriate initial treatment for this patient should be to ensure basic life support. Airway, breathing, and circulation should be maintained and other vital functions should be established. Vital signs and pertinent laboratory studies should be assessed including blood pressure, respiratory rate and volume, arterial blood gas, electrocardiography, glucose level and electrolytes, renal, liver function, coagulation tests and an acetaminophen level. The level of consciousness should be evaluated. Endotracheal intubation and assisted ventilation should be considered early to protect the airway. If the patient becomes seriously ill monitoring of urinary output, inserting a central line and pulmonary catheter for hemodynamic monitoring and emergency drug administration should be considered. It is critical that a pacemaker be readily available at the patient's bedside in all calcium channel blocker (CCB) ingestions. For patients presenting after known overdose or in any symptomatic patient, a poison center and cardiology consultation should be obtained as early as possible.

Gastrointestinal decontamination can be considered when appropriate; however no outcome data exists to support its use after CCB overdose. Induced emesis is not recommended in patients with CCB overdose because of the potential for hemodynamic instability and lack of documented efficacy. Activated charcoal and whole irrigation with high molecular weight polyethylene glycol such as GoLytely® or Colyte® are thought to be useful and in the absence of indications that they may cause harm and can be considered in select circumstances. In this patient, no gastrointestinal decontamination was recommended due to the late presentation time of greater than 4 hours and the expected decline in gastrointentional motility which may occur with CCB overdose.

Are any of the medications of concern in this patient?

Verapamil, especially the sustained release formulation, is by far the most concerning of the medications consumed and can be fatal in overdose. Sertraline, trazodone, and lorazepam may result in significant toxicity when taken in large amounts, though death is uncommon. A brief discussion of the agents that this patient took and their toxicity is provided below:

Sertraline – Zoloft®

Sertraline is a serotonin reuptake inhibitor used as an antidepressant. Serotonin is a chemical messenger that allows communication between nerves in the brain and the body. Depression has been associated with a decrease of synaptic serotonin in the brain. Sertraline works by improving symptoms of depression by increasing the availability of serotonin through decreasing re-uptake of serotonin centrally. Typical side effects of sertraline include dry mouth, blurred vision and dizziness. Palpitations, chest pain, and hypertension have also occurred. Most common signs and symptoms associated with overdose includes somnolence, nausea, vomiting, tachycardia, dizziness, agitation, and tremor. Sertraline is well absorbed through the gastrointestinal tract and reaches a peak level in 8-12 hrs. It has a large volume of distribution of 20 L/kg and has a high protein binding of 98%. The most consequential effect of sertraline is the serotonin syndrome. This manifests as agitation, delirium, hallucinations, mydriasis, hypertension, muscle rigidity and hyperthermia. Most patients with the serotonin syndrome recover following symptomatic and supportive care, particularly sedation with benzodiazepines and cooling if body temperature is elevated.

Trazodone – Desyrel®

Trazodone is use to treat depression and anxiety as a serotonin agonist. Common side effects of trazodone include dry mouth, nausea, vomiting, blurred vision, dizziness, headaches, lethargy and somnolence.

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A Fatal Ingestion

Continued from page 4

Sweating, weight change, and memory impairment have also been associated with its use. The most frequent manifestation of trazodone overdose is central nervous system depression, ranging from lethargy to coma. Nausea, vomiting and ataxia are also common. Trazodone is rapidly and completely absorbed, with peak levels occurring in 1/2 to 2 hours. It is 89% to 95% protein bound and has a volume of distribution of 1.27 L/kg. Symptomatic and supportive care is considered the basic management.

Lorazepam – Ativan®

Lorazepam is a benzodiazepine that is widely used for anxiety and seizures. Drowsiness, dizziness, loss of coordination, headache, nausea, and blurred vision may occur as side effects.. CNS depression, ataxia and slurred speech are common effects noted in patient who overdose. Benzodiazepines are generally of low toxicity unless ingested with other central nervous system depressants, such as ethanol. In these patients consequential respiratory depression may occur. Deaths from isolated overdose of benzodiazepines are extremely rare. The onset of action of lorazepam is 30-60 minutes. In regards to management, intubation and assisted ventilation are rarely indicated. Flumazenil is a specific benzodiazepine receptor antagonist. Flumazenil can reverse the sedative effects of benzodiazepines, however it is not always successful in reversing hypoventilation. Flumazenil may precipitate life threatening benzodiazepine withdrawal in dependent patients and for this reason its routine use is not recommended. Additionally, in the setting of concomitant cyclic antidepressant or other convulsant overdose, status epilepticus may occur.

Verapamil – Calan®, Isoptin®

Verapamil is a CCB. In sustained release forms, verapamil can cause serious toxicity or death after relatively small overdoses. Toxicity usually occurs 30 minutes to 6 hours after ingestion for an immediate release product, but controlled release preparations may not reach peak clinical effect until many hours after ingestion. Additionally, the duration of effect after overdose is extended. All symptomatic patients should be admitted to an intensive care unit for cardiac monitoring with a pacemaker readily available at the bedside.

How does Verapamil work?

Verapamil inhibits calcium ions from entering the "slow channels" or select voltage-sensitive areas of vascular smooth muscle and myocardium during depolarization. This both reduces the contractile force of the myocardium, reducing oxygen demand, and relaxes coronary vascular smooth muscle increasing myocardial oxygen delivery.. Peripherally, vascular smooth muscle relaxation occurs, lowering vascular resistance.

Which class of Calcium Channel Blockers does Verapamil belong to?

There are three classes of calcium channel blockers which include phenylalkylamines, benzothiazepines and dihydropyridines. A listing of the available agents available in the US with the recommended and maximum dosages, elimination half lifes, primary sites of action and toxicity is provided in Table 1 *(see page 6)*.

Verapamil is the only member of diphenylalkylamines that is currently approved in the United State and is the least selective of any CCB in terms of activity on the myocardium and vascular smooth muscle cells. It is used to treat high blood pressure, angina and supraventricular tachyarrhythmias. Diltiazem is the only member of the benzothiazepines that is currently approved in the United States. Like verapamil, diltiazem affects both heart and vascular smooth muscle cells. However, compared to verapamil, diltiazem has less prominent effects on the heart. It is also used to treat high blood pressure, angina and supraventricular tachyarrhythmias. The dihydropyridines include many newer agents such as amlodipine, felodipine, isradipine, and nicardipine. These second gernaration dihydropyridines are more selective for vascular smooth muscle cells. They are therefore particularly useful in the treatment of high blood pressure.

What are the clinical manifestations of CCB overdose?

Bradycardia and hypotension are main features of CCB overdose. Cardiac conduction abnormalities and complete heart block may also occur. These effects are seen particularly with verapamil and diltiazem. Neurological signs and symptoms may include dizziness, lethargy, coma, and seizure activity, however, many patients can remain alert even late in the course and with significant changes in vital signs. Nausea, vomiting, hyperglycemia and lactic acidosis can also occur.

What other interventions should be done to manage this patient's CCB toxicity?

- Intravenous lines should be placed and fluids should be infused to correct the blood pressure once adequate oxygenation, ventilation and appropriate airway protection are provided. Transcutanous pacing is usually not beneficial, but should be considered early possibly with

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A Fatal Ingestion

Continued from page 5

tranvenous pacing. Patients presenting with signs of significant hemodynamic instability should be managed at a facility capable of invasive cardiac monitoring and therapy.

- Calcium may improve depressed cardiac contractility, although its effects are often transient. Bolus doses of calcium can be administered intravenously over 5 minutes and repeated every 5 minutes until an effect is seen. Alternatively, calcium can also be administered with an initial bolus dose followed by a continuous calcium infusion. Depending on the formulation of the calcium salt, different doses are required. 10% Calcium chloride is preferred unless the patient has poor venous access or is pediatric due to

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Table 1 - Calcium Channel Blockers Available in the US

Drug	Usual adult dosage	Maximum adult daily dose (child)	Elimination half-life (hrs)	Indications	Primary site	Toxicity (therapeutic use)
Dihydropyridines						
Amlodipine (Norvasc®)	5-10mg orally once daily	>10mg (>0.3mg/kg)	30-50	high blood pressure, angina	vascular	headaches, peripheral edema
Felodipine (Plendil®)	5-10mg orally once daily	>10mg (0.3mg/kg)	11-16	high blood pressure	vascular	dizziness, headaches
Isradipine (Dynacirc®)	2.5-10mg orally every 12 hours	>20mg (0.1mg/kg)	8	high blood pressure	vascular	headaches, fatigue
Nicardipine (Cardene®, Carden SR®)	20-40mg orally every 8 hours	>40mg (IR) or 60mg (SR) (>1.25mg/kg)	2-4	high blood pressure, angina	vascular	headaches, peripheral edema, dizziness, flushing
Nifedipine (Procardia®, Adalat®)	20-40mg orally every 8 hour or 3-10 mcg/kg IV	>30mg (IR) or 120mg (SR) (any amount)	4	high blood pressure, angina	vascular	Low blood pressure, dizziness, flushing, nausea, constipation, edema
Nisoldipine (Sular®)	20-40mg orally daily	>30mg (any amount)	6-12	high blood pressure	vascular	Low blood pressure, dizziness, flushing, nausea, constipation, edema
Nitrendipine (Cardif®, Nitrepin®)	20mg orally once or twice daily	N/A	5-12	high blood pressure, angina (investigational)	vascular	Low blood pressure, dizziness, flushing, nausea, constipation, edema
Phenylalylyamine						
Verapamil (Calan®, Isoptin®),	80-160mg orally every 8 hours or 75-150 mcg/kg IV	>120mg (IR) or 480mg (SR) >2.5mg/kg	6 (immediate release)	high blood pressure, angina, arrhythmias	myocardium vascular	Low blood pressure, constipation, edema, bradycardia
Benzothiazepine						
Diltiazem (Cardizem®)	30-80mg orally every 60 hours or 75-150 mcg/kg IV	>120mg (IR) or 360mg (SR) (>1mg/kg)	3-4	high blood pressure, angina, arrhythmias	myocardium vascular	Low blood pressure, dizziness, flushing, bradycardia

Continued from page 6

the increased mEq/g of calcium (13.4 mEq Ca ++/1 g CaCl vs 4.3 mEq Ca ++/1 g calcium gluconate. Calcium chloride can be given as 10 ml (1 gram) in a dosage of 0.2-0.4 ml/kg per hour. Alternatively, 10% Calcium gluconate can be given in a dose of 30 ml (3 grams) at a rate of 0.6-1.2 ml/kg per hour.

- Although atropine had been used in for bradycardia or heart block in some reported cases in doses up to 2 mg intravenously, there are many cases reported where it is ineffective in managing cardiovascular toxicity secondary to calcium channel blocker overdose.
- Intravenous insulin with supplemental dextrose and potassium can reverse significant and persistent hypotension and bradycardia and should be considered early in the management of CCB overdose. Insulin has positive inotropic effects and can increase coronary blood flow and myocardial oxygen delivery. An intravenous insulin bolus of 1 U/kg followed by a continuous drip of 0.5 U/kg per hour can be given and adjusted as required. Onset of response is delayed for approximately 20-30 minutes. Twenty five grams of IV dextrose is administered to prevent hypoglycemia and adjusted as needed. The glucose level must be followed closely; monitoring should continue for 6 hours after the insulin infusion is stopped because late-onset hypoglycemia is reported. Intracellular shifts of potassium may also occur as a result of insulin-dextrose infusions; therefore patients should also be monitored for hypokalemia.
- Vasopressors such epinephrine, norepinephrine and dopamine can help reverse a low blood pressure and depressed heart rate. Invasive hemodynamic monitoring is imperative to guide the appropriate selection of vasopressor agent. Norepinephrine is the preferred vasopressor; it enhances the calcium channels of vascular smooth muscle and can cause a significant increase in systemic vascular resistance. Dopamine exerts its effects by stimulating the release of norepinephrine, but has not proven to produce a predictable response after CCB overdose.
- Glucagon has been used to treat calcium channel blockers toxicity with varying rates of success. Glucagon promotes calcium influx causing stimulation of the heart. It can be given as an intravenous bolus of 1-10 mg in adults followed by a constant infusion of 0.1 mg/kg per hour and titrated as needed.
- Vasopressin is reported in single case reports to be successful in improving blood pressure in patients with dihydropyridine CCB poisoning. Vasopression works through enhancement of the V-1 receptor-mediated vasoconstrictive effects. In patients recalcitrant to standard care high doses may be required and models in animals have been conflicting.
- Amrinone is a phosphodiesterase inhibor which will increase CAMP through decreasing it's metabolism. It's use should be carefully monitored due to the propensity of this drug to produce hypotension.

What about the non-responding patients?

Patients persistently unresponsive, should be considered for placement of an intraaortic balloon pump. Placement should be conducted while the patient has a blood pressure which can support this placement. Early consultation with cardiology should occur to facilitate this process and once placed, other therapeutic medications should be continued until no longer required.

Are there any medications that should be avoided in this patient during treatment?

Avoid concurrent administration of medications which depress cardiac conduction or myocardial contractility because they may enhance toxicity. These agents include amidarone, antihistamines such as diphenhydramine, beta-blockers, cyclic antidepressants, disopyramide, propoxyphene, procainamide, and quinidine.

How toxic are the other medications that this patient ingested?

The other medications taken by this patient included lisinopril, hydrochlorothiazide, and finasteride. These agents are usually considered relatively benign in overdose. They are briefly reviewed below:

Lisinopril – Zestril®

Lisinopril belongs to a group of medication known as ACE inhibitors. ACE inhibitors are used to treat high blood pressure via widening the blood vessels by blocking a potent vasoconstrictor in the body. Common side effects of this medication include headache, dizziness, lightheadedness, fatigue, nausea, diarrhea, dry cough and blurred vision. Acute overdose results in mild hypotension and transient renal insufficiency. Treatment is symptomatic and supportive.

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A Fatal Ingestion

Continued from page 7

Hydrochlorothiazide

Hydrochlorothiazide is a thiazide diuretic that is used in the treatment of high blood pressure. It works by eliminating the excess fluids in the body by blocking the re-absorption of sodium and water. Dizziness, lightheadedness, headache, blurred vision, stomach upset, diarrhea, and constipation are possible side effects associated with the use of this drug. The toxicity associated with acute and chronic overdose of diuretics is primarily related to fluid and electrolyte loss. Toxicity can be corrected with the appropriate fluids.

Finasteride – Proscar®

Finasteride is use for the treatment of enlarged prostate also known as benign prostatic hyperplasia. Dihydrotestosterone is a natural body hormone that causes growth of the prostate. Finasteride works by decreasing the amount of dihydrotestosterone. This results in improving symptoms such as the urge to urinate and helps to ease the flow of urine by decreasing the need to strain. Common side effects of this medication may include a decrease in sexual energy and an increase in hair growth. An acute overdose of 80 times the recommended daily dose and chronic exposure of 16 times the recommend daily dose have been tolerated by patients without producing any adverse effects.

Hospital course

Initial management provided to the patient before the Poison Center was called consisted of intravenous atropine for bradycardia and 6 mg of intravenous naloxone for respiratory depression, which produced no response. Shortly after admission the patient became hypoxic and comatose. The Poison Center recommended endotracheal intubation and assisted ventilation to protect the airway and to use a pacemaker. The following drugs were also recommended to help support his low heart rate and blood pressure: intravenous calcium gluconate, insulin, glucose, glucagon and vasopressors. Over the next few hours, the patient's condition rapidly deteriorated and he expired 11 hours later. After the autopsy, the cause of death was identified as an acute overdose due to mixed drugs. Toxicology analysis revealed the following post-mortem serum levels after the autopsy: **verapamil** 1.61 micrograms/ml (toxic: >0.845 micrograms/ml and fatal: >2 micrograms/ml); **sertraline** 1.05 micrograms/ml; nor-sertraline 1.11 micrograms/ml; (fatal levels of sertraline have been reported at 0.23-1 micrograms/ml); **trazodone** 0.72 micrograms/ml (therapeutic: 0.5-2.5 micrograms/ml, toxic > 2.5 micrograms/ml)

OTHER ISSUES RELATED TO CALCIUM CHANNEL BLOCKER INGESTIONS

When should a patient be referred to the emergency department after the ingestion of a calcium channel blocker?

Recently, an evidence based consensus guideline for the management of calcium channel blockers was published by the American Association of Poison Control Centers.

According to this consensus guidelines, a patient should be referred into an emergency department under the following conditions:

- If self harm, suicidal or malicious intent suspected
- If patient is symptomatic with signs of weakness, dizzy, or syncope
- If ingestion within 6 hours for immediate release products, 18 hours for extended release products, 24 hours for extended release formulation of verapamil
- If a patient has underlying cardiovascular disease or is taking another cardio-depressant drug such as a beta-blocker
- If a patient is living alone or if the family members are unavailable
- If unable to estimate the amount ingested or the ingested amount is above the maximum recommended daily dosage

References:

1. *Anderson AC. Calcium Channel Blocker Overdose. Journal of Clinical Pediatric Emergency Medicine 2005; 109-15.*
2. *Spiller HA, Meyers A, Z1emba T et al: Delayed onset of cardiac arrhythmias from sustained-release verapamil. Ann Emerg Med 1991; 20:201-3.*
3. *Tom PA, Morrow CT, Kelen GD: Delayed hypotension after overdose of sustained release verapamil J Emerg Med 1994; 12:621.*
4. *Belson MG, Gorman SE, Heller RJ: Calcium Channel Blockers ingestion in children Clinical Toxicol 1998; 36:310.*
5. *Salhanick SD, Shannon MW. Management of calcium channel antagonist overdose. Drug Safety 2003; 26:65-79.*
6. *Olson KR, Erdman AR, Woolf AD, et al. Calcium Channel Blocker Ingestion: An Evidence-Based Consensus Guideline for Out-of-Hospital Management. Clinical Toxicology 2005; 43:797-822.*
7. *American Heart Association. Management of Cardiac Arrest. Part 7.2 Circulation 2005;112:IV:58-IV:66 Originally published online Nov. 28. 2005*

SPI CORNER:

THE CASE OF THE WOMAN WHO BECAME SICK FROM HER GARDEN

Contributed By: Ka Wing (Carmen) Lee, PharmD. Candidate. St. John's University, T Caraccio, Pharm.D., ABAT, J Flori, RN, CSPI, J Leonard, RN, CSPI, Long Island Regional Poison and Drug Information Center at Winthrop University Hospital, Mineola, NY

A 27 year-old woman presented to the hospital because of altered mental status and anxiety. The previous evening, the patient had a normal dinner with her husband. After dinner, she started to feel queasy and lightheaded. She also felt weak, sick, and hot. The husband quickly took his wife to the hospital because she seemed anxious. When she spoke random and meaningless words came out. The patient had no significant past medical history except for depression for which she was taking paroxetine and amitriptyline. On arrival in the hospital, the patient's blood pressure was high and her heart rate was 150 beats per minute. She had no fever, but her mucous membrane was dry and her skin was warm and she was very sensitivity to light. The rest of her physical examination was normal. Upon questioning the husband, he told the doctor that he also felt funny the night before. He felt "nauseated, jittery and his heart was racing" but his symptoms quickly resolved within a few hours. After four days, the patient recovered; her blood pressure came down, she was less confused and her speech was cleared, but the doctor was not able to find the cause of her symptoms. One afternoon as the patient went outside to do some gardening she noticed that there were several strikingly beautiful white and yellow flowers next to the lettuce which she was growing. Both her and her husband had eaten this lettuce on the night that she had become sick. She pulled the plant out and went to a nursery, where it was identified as jimson weed. As it turned out, the patient's symptoms were due the toxicity cause by the jimson weed that had somehow gotten mixed into her salad*.

SPI Comments: All parts of the Jimson Weed (Datura stramonium) plant are considered toxic. Ingestion of only a few leaves or seeds may produce toxicity, as demonstrated in this case. This patient presented with the classic symptoms of jimson weed poisoning: mad as a hatter, blind as a bat, dry as a bone, red as a beet. Management consists of providing symptomatic and supportive care.

**Case reported by Sanders L. Flower Power NY Times 5.21.06 Http://www.nytimes.com/2006/05/21/magazine/21wwln_diagnosis.html?_r=1&oref=slogin*

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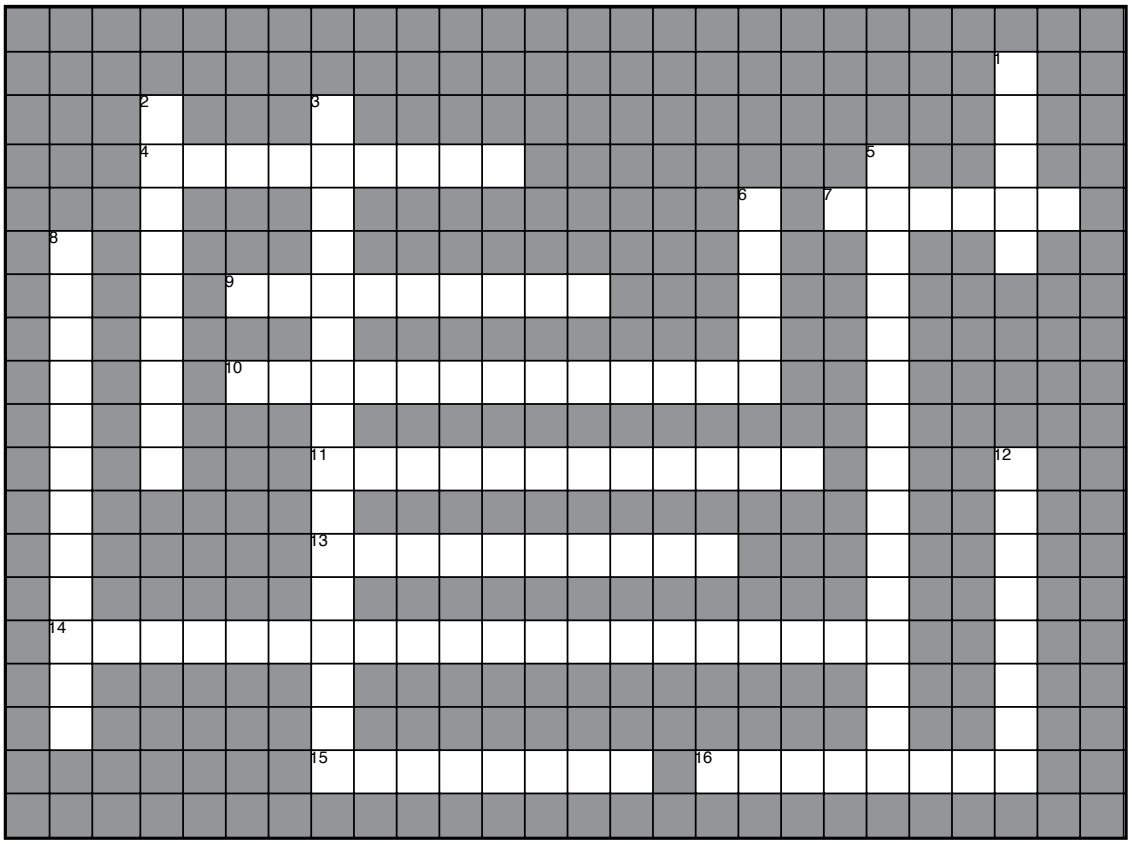
TOXICOLOGY CROSSWORD
FOOD AND FISH POISONING

Contributed by: Mary Halsey-Claps, RN, CSPI, Upstate New York Poison Control Center, Syracuse, NY



Across

4. The "hot to cold" sensation (and the reverse) is associated with which type of fish poisoning?
7. Which organ can be seriously affected in the very young if they eat unpasturized apple juice or raw meat and develop the Hemolytic uremic syndrome?
9. Saxitoxin is the name of the toxin responsible for producing which type of Shellfish poisoning?
10. The first outbreak of Amnestic shellfish poisoning in 1987 occurred from shellfish located in river estuaries on which Island in the North East?
11. What is the name of the deadly toxin found in the puffer fish?
13. Which bacteria can produce stomach pain, diarrhea, nausea, chills, fever and headaches usually in 8-72 hours from undercooked eggs, poultry, meat and diary products?
14. Which toxin affects the nervous system and can be produced from improperly canned foods?
15. What is the name of the colorful tropical fish that has long spines on it that produce intense pain on contact?
16. Pregnant woman, newborn, elderly and people with weakened immune systems can become seriously ill from eating contaminated deli-styled meats and poultry. The last part of the name of the causative organism ends in monocytogenes. What is the first part of the name of this organism?

Down

1. What is the name of the fruit that has been associated with features of the Jamaican vomiting illness which can produce severe vomiting and hypoglycemia if the unripe form if consumed?
2. Which fish poisoning produces a histamine-like reaction within 30-60 minutes after eating spoiled fish?
3. The Staphylococcus aureus toxin can rapidly multiply at room temperature and primarily affect which organ system within 6 hours?
5. What is the generic name of a common OTC drug that is useful to treat symptomatic patients with Scombroid fish poisoning?
6. Which organ may require artificial support in a severe tetrodotoxin poisoning?
8. Which organ system can be affected for several weeks or longer from Ciguatera fish poisoning?
12. What can multiply rapidly between 40°F and 140°F and is commonly responsible for producing many types of Food borne illness?

Answers: Across: 4. Ciguatera; 7. Kidney; 9. Paralytic; 10. Prince Edwards; 11. Tetrodotoxin; 13. Salmonella; 14. Clostridumbotulinum; 15. Lionfish; 16. Listeria. **Down:** 1. Ackee; 2. Scombroid; 3. Gastrointestinal; 5. Diphenhydramine; 6. Lungs; 8. Neurological; 12. Bacteria.

New York State Poison Centers
1-800-222-1222

October 2006

The NY State Poison Centers

TOXICOLOGY LETTER

A Quarterly Publication • Vol. XI No. 4

Program Announcements • •

Ruth A. Lawrence: Monthly conference: every 4 weeks on Thursdays (11 am to noon), and every 4 weeks on Tuesdays (10 am-11 am).

CNY: Our **Tenth Annual Toxicology Teaching Day** on November 15, 2006 at the Sheraton in Syracuse. Please contact Rose More *morer@upstate.edu* for more information.

NYC: Consultants Case Conference • The first Thursday of the Month from 2-4pm

LI: Pre-Registration is required. Please contact Mr. Denis Jao at 516-663-2650 to register.

Both Telephone and Televideo broadcasts will be available.

Target Audience: Physicians, Pharmacists, Nurses, Physician-Assistants, Laboratory technicians, EMS staff, medical/nursing/pharmacy students and other healthcare professionals. CME Credits are being applied for Nurses, Pharmacists and Physicians and Physician-Assistants.

Location: New Life Conference Rooms B&C
Winthrop-University Hospital
259 First Street
Mineola, Long Island, New York 11501

Times for ALL Conferences are: 12:15 PM-1:45 PM

Tuesday, October 31, 2006 TOPIC: **"THE TEN MOST SIGNIFICANT ARTICLES PUBLISHED IN TOXICOLOGY IN THE LAST 2 YEARS"**

Speaker: Gar Chan, MD, ABEM., North Shore University Hospital, Manhasset, NY. Attending Physician, Department of Emergency Medicine

Tuesday November 28, 2006 TOPIC: **"HOW TO EVALUATE AND TREAT THE POISONED PATIENT"**

Speaker: Matthew Carman, MD, State University of New York at Stony Brook, NY. Senior Resident, Department of Emergency Medicine

Please call administrative telephone numbers for more information.

Isoniazid Poisoning Case Report:

Contributed by: Alex Manini, MD, Fellow in Medical Toxicology, New York City Poison Control Center, New York, NY

A 16-year-old girl was brought into the emergency department (ED) by ambulance with an ongoing tonic-clonic seizure. Emergency Medical Services was called after her family found her convulsing on the floor at home. According to the family, she had no prior seizure disorder and took no medicines regularly. Paramedics established intravenous access and administered 25 grams of dextrose without any effect. She convulsed continuously for approximately 30 minutes prior to arrival in the ED. Immediately upon arrival, the emergency physician administered 2 milligrams of intravenous lorazepam that rapidly terminated the seizure.

On arrival to the ED, she was unarousable and unresponsive. She was attached to a cardiac monitor. Her initial vital signs were: blood pressure, 130/70 mmHg; pulse, 120 beats per minute; respirations, 16 breaths per minute; rectal temperature, 98.0° Fahrenheit; oxygen saturation, 100% on room air. Her skin was warm and diaphoretic. There was no evidence

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Toxicology Advice Centers • •

Administrative Phone Numbers - To obtain a consult in your area, call 1.800.222.1222.

Western New York Poison Center (WNY)
716.878.7871 • http://wnypoison.org

Ruth A. Lawrence Poison and Drug Information Center Serving the Finger Lakes Region (FL)
585.273.4155 • www.FingerLakesPoison.org

Upstate New York Poison Center (UNY)
315.464.7078 • www.cnypoison.org

New York City Poison Control Center (NYC)
212.447.8152

Long Island Poison & Drug Info Center (LI)
516.663.4574 • www.LIRPDIC.org

Dietary Supplements Containing Ephedrine Alkaloids

FDA informed consumers and healthcare professionals that all dietary supplements containing ephedrine alkaloids are illegal to market in the United States. *Aug 21, 2006*

Dexedrine (dextroamphetamine sulfate)

The FDA and GlaxoSmithKline notified healthcare professionals of changes to the BOXED WARNING, WARNINGS and PRECAUTIONS sections of the prescribing information for Dexedrine (dextroamphetamine sulfate), approved for the treatment of Attention-Deficit Hyperactivity Disorder and narcolepsy. The warnings describe reports of sudden death in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. *August 04, 2006*

Unapproved Compounded Inhalation Drugs

The FDA notified consumers and healthcare professionals that RoTech Healthcare, Inc., CCS Medical, and Reliant Pharmacy Services are manufacturing and distributing unapproved compounded inhalation drugs nationwide. *August 10, 2006*

Hydralazine HCl Injection, USP, 20 mg/mL

Luitpold Pharmaceuticals, Inc. and FDA notified healthcare professionals of a voluntary recall of additional lots of Hydralazine HCl Injection (20 mg/mL, 1 mL single dose vials) because the products may contain particulates. *August 11, 2006*

WellPatch Cough & Cold Soothing Vapor Pads

The Mentholatum Company and FDA notified consumers and healthcare professionals about a nationwide recall of WellPatch Cough & Cold Soothing Vapor Pads due to potential serious adverse health effects that could result if the product is ingested by a child removing the patch and chewing on it. This product contains camphor, eucalyptus oil, and menthol. *August 01, 2006*

High-Strength Hydrogen Peroxide

FDA warned consumers not to purchase or to use high-strength hydrogen peroxide products, including a product marketed as "35 Percent Food Grade Hydrogen Peroxide," for medicinal purposes because they can cause serious harm or death when ingested. *July 27, 2006*

Ultravist (iopromide) Injection 370mgI/mL, 125 mL

Berlex, Inc. and FDA announced a voluntary worldwide recall of all lots of Ultravist (iopromide) Injection 370mgI/mL, 125 ml, due to the presence of particulate matter and crystallization with the potential for thromboembolic safety problems if an affected product is administered to patients. *July 31, 2006*

Bismacine/Chromacine

FDA notified healthcare professionals and consumers not to use an injectable product called Bismacine, also known as Chromacine. Bismacine is not a pharmaceutical and has not been approved to treat any condition; however, it is being prescribed or administered by doctors of "alternative health" to treat Lyme disease. This product contains high amounts of bismuth, a heavy metal that is used in some medications taken by mouth to treat Helicobacter pylori, a bacteria that can cause stomach ulcers. *July 21, 2006*

SSRIs and Treatment Challenges of Depression in Pregnancy

FDA notified healthcare professionals and consumers of important information from two recent studies that should be considered when making treatment decisions in pregnant women who take antidepressants. The studies included pregnant women who were treated with selective serotonin reuptake inhibitors (SSRIs), or in a few cases, other antidepressant medications.

One study illustrated the potential risk of relapsed depression after stopping antidepressant medication during pregnancy. In this study, women who stopped their medicine were five times more likely to have a relapse of depression during their pregnancy than were women who continued to take their antidepressant medicine while pregnant.

The second study suggests there may be additional, though rare, risks of taking SSRI medications during pregnancy. This study focused on newborn babies with persistent pulmonary hypertension

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(PPHN), which is a serious and life-threatening lung condition that occurs soon after birth. Babies born with PPHN have high pressure in their lung blood vessels and are not able to get enough oxygen into their bloodstream. In this study, PPHN was six times more common in babies whose mothers took an SSRI antidepressant after the 20th week of pregnancy compared to babies whose mothers did not take an antidepressant. The study was too small to compare the risk of one drug compared to another. The finding of PPHN in babies of mothers who used a SSRI antidepressant in the second half of pregnancy adds to concerns from previous reports that infants of mothers taking SSRIs late in pregnancy may experience difficulties such as irritability, difficulty feeding and in very rare cases, difficulty breathing.

Additionally, the labeling for paroxetine (Paxil) was recently changed to add information about findings in an epidemiologic study that suggests that exposure to the drug in the first trimester of pregnancy may be associated with an increased risk of cardiac birth defects. *July 19, 2006*

5-Hydroxytryptamine Receptor Agonists (Triptans)

Selective Serotonin Reuptake Inhibitors (SSRIs)

Selective Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)

Serotonin Syndrome

FDA notified healthcare professionals and consumers of new safety information regarding taking medications used to treat migraine headaches (triptans) together with certain types of antidepressant and mood disorder medications (selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs). A life-threatening condition called serotonin syndrome may occur when triptans are used together with a SSRI or a SNRI. *July 19, 2006*

Azathioprine Tablets, 50 mg

Roxane Laboratories and FDA notified pharmacists and other healthcare professionals of a nationwide recall of a single manufacturing lot of Azathioprine tablets, 50 mg (Lot 558470A, Exp Mar 2009) used to help prevent rejection in kidney transplant patients, and to manage severe rheumatoid arthritis. The recall was initiated due to concerns that bottles from this single lot # 558470A, labeled as Azathioprine may contain Methotrexate, 2.5 mg tablets. *July 13, 2006*

Dietary Supplements Promoted for Sexual Enhancement

The FDA notified healthcare professionals and consumers of a warning not to purchase or consume Zimaxx, Libidus, Neophase, Nasutra, Vigor-25, Actra-Rx, or 4EVERON, illegal drugs with undeclared ingredients that are promoted and sold on web sites as "dietary supplements" for treating erectile dysfunction and enhancing sexual performance. *July 12, 2006*

Aptivus (tipranavir)

Boehringer Ingelheim and FDA informed healthcare professionals of important new safety information for Aptivus (tipranavir) capsules, co-administered with ritonavir (500mg/200mg), that includes an addition to the drug's Black Box Warning regarding reports of both fatal and non-fatal intracranial hemorrhage (ICH). *June 30, 2006*

Ketek (telithromycin)

The Food and Drug Administration notified healthcare professionals and patients that it completed its safety assessment of Ketek (telithromycin), indicated for the treatment of acute exacerbation of chronic bronchitis, acute bacterial sinusitis and community acquired pneumonia of mild to moderate severity, including pneumonia caused by resistant strep infections. The drug has been associated with rare cases of serious liver injury and liver failure with four reported deaths and one liver transplant after the administration of the drug. *June 29, 2006*

Triaminic Vapor Patch

Novartis Consumer Health and FDA notified patients, pharmacists and other healthcare professionals that the sponsor is conducting a nationwide voluntary recall of all Triaminic Vapor Patch products due to reports of serious adverse events associated with accidental ingestion by children. *June 20, 2006*

Continued from page 1

of head trauma. Pupils were 4mm, equal, round and reactive to light. The lungs were clear and her heartbeat was regular and without murmurs. Her abdomen was soft and non-distended. She had strong and equal distal pulses, and there was no peripheral clubbing, cyanosis, or edema.

An electrocardiogram was performed which revealed sinus tachycardia with a leftward axis, QRS duration of 90 milliseconds, no evidence of myocardial ischemia, absence of an R wave in lead aVR (essentially ruling out tricyclic antidepressant poisoning), and a QTc interval of 430 milliseconds. Laboratory testing results, sent shortly after termination of her seizure, revealed a bicarbonate of 8 mEq/L, an elevated anion gap of 34 mEq/L, glucose of 406 mg/dL, lactate of 9 mmol/L, normal creatinine and normal coagulation studies. Bedside urinalysis from a catheter specimen was negative.

What causes status epilepticus following poisoning?

A seizure is defined as uncontrolled brain activity (generally measured with electroencephalography), whereas a convulsion is the outward motor manifestation of this excessive brain activity. The most common form of convulsion is tonic-clonic in nature, in which periods of convulsive activity are interspersed with periods of high tone. In clinical practice the terms seizure and convulsion are often used interchangeably, and the term tonic-clonic is often assumed. This patient had, by definition, status epilepticus (SE) because she demonstrated continuous motor seizure activity for greater than 15 minutes.[1]

Although the differential diagnosis of seizure following poisoning is exceptionally broad,[2] the list of poisons that routinely cause SE is more limited. Hypoglycemics, such as sulfonylureas and insulin, can cause SE secondary to persistent hypoglycemia.[3] Carbon monoxide can cause SE due to decreased brain oxygen delivery with resultant tissue hypoxia,[4] as well as via inactivation of mitochondrial cytochrome oxidase which leads to oxidative stress in the brain[5] and release of excitatory neurotransmitters.[6] Methylxanthine overdose (e.g. theophylline, caffeine) can cause refractory SE due to antagonism of adenosine,[7] the endogenous inhibitory neurotransmitter responsible for halting seizures.[8] Hydrazides (e.g. isoniazid) and methylated hydrazines (such as those found in rocket fuels, alternative medicine and *Gyromitra* mushrooms) inhibit conversion of the neurotransmitter glutamate (excitatory) to GABA (inhibitory),[9] leading to excess neuroexcitation. Cicutoxin, produced by water hemlock (*Cicuta maculata*), is a potent inhibitor of GABA neurotransmission that likewise reduces inhibitory tone.[10] And finally, bupropion can also cause refractory SE by an undefined mechanism, but probably mediated by action of its metabolite, hydroxybupropion.[11]

Case Continued:

The family arrived to the ED shortly thereafter and brought with them an empty pill bottle of isoniazid (INH). It was her sister's prescription that she had filled the day prior for a newly positive PPD after a trip to South America. There were 30 pills (300 milligrams each) missing, or a maximum potential ingestion of 9 grams. Over the course of the next hour in the ED, the patient's mental status had not improved significantly and she had two additional generalized seizures, each of which responded to 2 milligrams of lorazepam.

What is the mechanism of isoniazid-induced seizures?

Under normal conditions, neurotransmitters in the central nervous system maintain a balance between excitation and inhibition. In a patient with an acute overdose of INH, this balance is disrupted and a milieu that favors an excess of excitation is produced. INH metabolism products called hydrazones inhibit pyridoxine phosphokinase,[12] the enzyme responsible for production of pyridoxal 5' phosphate (P5P) from pyridoxine (a.k.a. vitamin B6). In addition, INH directly inactivates P5P. Since P5P is an important cofactor in the enzymatic conversion of glutamate to GABA by glutamate decarboxylase, the combined effects of INH on P5P function prevent the synthesis of sufficient quantities of GABA.[9] Seizures occur because of both a deficiency of GABA and an excess of glutamate (due to prevention of metabolism to GABA).

How are patients with toxicologic seizures managed?

Once a readily treatable cause of seizure such as hypoxia or hypoglycemia is excluded, intravenous benzodiazepines, such as diazepam (5-10 milligram boluses) or lorazepam (1-2 milligram boluses), are the first-line anticonvulsants.[13] Failure to terminate or recurrence despite adequate therapy often suggests the need for a second line agent such as barbiturates, phenytoin, or propofol.[13] Barbiturates or related agents such as propofol, while generally successful at seizure control, produce significant respiratory depression and typically mandate consideration of airway protection with endotracheal intubation. Phenytoin, a sodium channel blocker that inhibits saltatory conduction of

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excitatory impulses from an anatomical seizure focus, is less useful in toxicologic seizures than other second line agents.

For patients with SE in whom overdose is an etiologic consideration, or in those with likely access to isoniazid, pyridoxine (vitamin B6) should be administered empirically. The specific timing of its administration depends on the likelihood of the overdose and on the response to initial therapy. That is, patients who fail to respond to an appropriate dose of benzodiazepine, in whom overdose is a consideration, should probably receive empiric therapy with pyridoxine prior to advancing to barbiturates. The dose is 70 milligrams per kilogram up to an initial dose of 5 grams, with repeat doses as necessary to equal the suspected amount of INH ingested in grams.[14] Pyridoxine itself can be toxic in high doses (typically greater than 350 milligrams per kilogram) and care should be taken not to administer more than the "gram of pyridoxine per gram of INH" limit.[15] Diazepam and pyridoxine are synergistic and should be used together.[16] Coma after large INH overdose may also respond to pyridoxine (reported in 3 patients).[17]

Case Resolution

The patient received an initial dose of 5 grams pyridoxine over 30 minutes, with instructions from Poison Control to redose with pyridoxine (at up to 500 milligrams per minute) if seizures recurred. Serum toxicology screens for salicylates and acetaminophen were also recommended given the suicidal nature of the overdose. As the nurse was hanging the pyridoxine, the patient experienced another seizure. The emergency physician infused the pyridoxine infusion "wide-open" for one minute and the seizure resolved without administration of additional benzodiazepines. Prior to transfer to the pediatric intensive care unit (PICU), another seizure occurred and three 500-milligram "boluses" of pyridoxine were administered, again with good effect.

In the PICU, 2.5 grams of additional pyridoxine (for a total of 9 grams) were infused and no further seizures recurred. The patient's mental status returned to normal within 24 hours. Computed tomography of the head was normal. Serum screens for salicylates and acetaminophen were negative. On further questioning the next day, the patient admitted to a suicide attempt with her sister's INH and she was subsequently medically cleared for evaluation by the psychiatry service.

References

1. *Lowenstein D, Bleck T, MacDonald R. It's time to revise the definition of status epilepticus.* **Epilepsia**. *1999; 40: 120-122.*
2. *Rao, R: Neurologic principles. In: Flomenbaum NE, Goldfrank LR, Hoffman RS, Howland MA, Lewin NA, Nelson LS, eds: Goldfrank's Toxicologic Emergencies 8th ed., 2006, pp 312-313.*
3. *Malouf R, Brust JC. Hypoglycemia: causes, neurological manifestations, and outcome.* **Ann Neurol**. *1985; 17: 421-430.*
4. *Roughton FJW, Darling RC. The effect of carbon monoxide on the hemoglobin dissociation curve.* **Am J Emerg Med**. *1944; 141: 17-31.*
5. *Thom SR, et al. Dehydrogenase conversion to oxidase and lipid peroxidation in brain after carbon monoxide poisoning.* **J Appl Physiol**. *1992; 73: 1584-1589.*
6. *Zhang J, Piantadosi CA. Nitric oxide mediates excitotoxicity induced by carbon monoxide poisoning in rat brain.* **Undersea Hyperbaric Med**. *1995; 22: 16.*
7. *Friedholm BB. Theophylline actions on adenosine receptors.* **Eur J Respir Dis**. *1980; 109 (Suppl): 29-36.*
8. *Eldridge FL, Paydarfar D, Scott SC, Dowell RT. Role of endogenous adenosine in recurrent generalized seizures.* **Exp Neurol.** *1989; 103: 179-185.*
9. *Wood JD, Peesker SJ. The effect on GABA metabolism of isonicotinic acid hydrazide and pyridoxine as a function of time after administration.* **J Neurochem**. *1972; 19: 1527-1537.*
10. *Blythe WB. Hemlock poisoning, acute renal failure, and the Bible.* **Ren Fail**. *1993; 15: 653.*
11. *Davidson J. Seizures and bupropion: a review.* **J Clin Psychiatr.** *1989; 50: 256-261.*
12. *Miller J, Robinson A, Percy AL. Acute isoniazid poisoning in childhood.* **Am J Dis Child**. *1980; 134: 290-292.*
13. *Kalviainen R, Eriksson K, Parviainen I. Refractory generalized convulsive status epilepticus: a guide to treatment.* **CNS Drugs**. *2005; 19 (9): 759-68.*
14. *Wason S, Lacouture PG, Lovejoy FH. Single high-dose pyridoxine treatment for isoniazid overdose.* **JAMA**. *1981; 246: 1102-1104.*
15. *Schaumburg H. Sensory neuropathy from pyridoxine abuse.* **N Eng J Med**. *1984; 310: 198.*
16. *Chin L, Sievers ML, Herrier RN, et al. Potentiation of pyridoxine by depressants and anticonvulsants in the treatment of acute isoniazid intoxication in dogs.* **Toxicol Appl Pharmacol**. *1981; 58: 504-509.*
17. *Brent J, Vo N, Kulig K, Rumack BH. Reversal of prolonged isoniazid-induced coma by pyridoxine.* **Arch Intern Med**. *1990; 150: 1751-1753.*

SPI CORNER: HOLIDAY POISONINGS

Contributed by: Laureene Piwinski, Rn, CSPI, Upstate NY Poison Center

Now that the back-to-school rush is over and autumn is upon us, many people are turning their thoughts to the upcoming holiday season. With the hustle and bustle of preparing for and celebrating the holidays, it's easy to overlook the poisoning hazards that are unique to theses special times. In addition to the temporary household toxins that are present during certain holidays, sometimes holiday stress can result in people overlooking routine safety precautions

In a very short time Halloween will be here. While the kids are enjoying the spooky atmosphere, parents sometimes have real fears associated with their little ones on this holiday. The following are common Halloween exposures and concerns.

- Glow jewelry consists of plastic tubing that contains small quantities of dibutyl phthalate, a nearly colorless oily liquid. It is mildly irritating to the eyes, but oral and dermal exposures generally do not result in symptoms. Rinse and dilute is the standard treatment to these exposures. Occasionally, older children and teens may swallow small intact glow sticks that they place in their mouths for theatrical effect. This should be treated as a foreign body exposure and as a potential choking hazard.
- Flashing jewelry contains tiny disc batteries that may cause caustic injury when ingested. When a disc battery aspiration is suspected, referral to an emergency room is indicated as well as close follow up to be sure that the battery passes without incident.
- Make-up, while considered to be non-toxic, may cause irritation or an allergic reaction to a child's skin. If irritation or a rash occurs, wash the affected area well with soap and water and seek medical attention as needed.
- Candy and other edible treats may also present a hazard to children. Parents should be warned to check every item carefully for potential tampering before the child is allowed to eat it. Only treats that are in their original intact wrappers should be eaten. Fruit, such as apples, need to be washed thoroughly and cut into small pieces before being given to children. Discard homemade treats if you do not know the person who gave them to your child.

Thanksgiving, New Year's Eve, and New Years days pose some similar poisoning risks for adults and children, due to having holiday guests and parties.

- Drug exposures may occur when visiting guests bring their medications with them in their, purses, pockets, or suitcases, sometimes not in their original containers. Caregivers may also be more forgetful about keeping their own medications out of the reach or children or be more likely to skip or take double doses of their own medications when distracted by the holiday atmosphere. Treatment for these exposures is determined by the specific medications and amounts, or they may have to be treated as an unknown medication if this information is not available.
- Food poisoning may result from eating undercooked food or food that has been left at room temperature for more than 2 hours. In healthy children and adults many types of food poisoning that cause gastroenterological symptoms are self-limiting and require no treatment other than fluid replacement. If symptoms are severe, or persist for more than 24 hours, people should be referred to an emergency facility. Young children, elderly people, and people who are immunosuppressed are at higher risk for systemic complications and treatment recommendations should be more aggressive in these populations.
- Unfinished alcoholic beverages that are not immediately discarded pose a risk for curious children. Children are more susceptible than adults are to hypoglycemia after ethanol consumption, which may them at a risk for seizures. Adults may intentionally drink more alcohol than they are accustomed to during the holidays resulting in alcohol toxicity or injury to themselves or others.
- Nicotine containing products are also more commonly found in homes during the holidays, putting children at risk for nicotine toxicity. Children ingesting 1 or more whole cigarettes, 3 or more cigarette butts, nicotine patches or gum, or who develop symptoms of exposure other than vomiting should immediately be referred to an emergency room.

Continued on page 8

WORD SEARCH

COMMON PITFALLS IN OD MANAGEMENT

Contributed by Michelle Valerino, RN, Upstate NY Poison Center

J	E	H	Y	P	E	R	B	A	R	I	C	T	H	I	N	A	S	V	Y	I	B	O	T	O	B
O	N	C	E	F	G	A	S	D	F	G	H	J	K	L	U	I	O	C	R	V	E	B	E	T	E
S	I	A	D	T	L	N	D	B	O	W	E	L	S	O	U	N	D	S	T	V	T	W	A	I	N
G	M	R	B	O	W	U	N	B	V	G	H	J	M	R	E	F	G	H	E	Y	A	A	M	S	Z
J	G	D	N	K	N	A	M	E	O	F	T	H	E	G	A	M	E	S	M	I	B	M	L	Y	O
F	I	I	Y	P	O	D	I	A	S	T	O	F	T	E	L	E	V	I	I	O	L	Z	O	S	D
N	T	O	F	O	M	E	P	I	Z	O	L	E	H	O	L	D	B	X	X	O	O	A	D	T	I
N	S	T	A	S	O	C	K	S	R	E	D	R	A	G	O	N	B	O	O	B	C	T	L	O	A
F	O	O	J	I	G	A	L	S	X	I	N	A	N	S	H	O	P	P	E	R	K	L	A	L	Z
I	S	X	L	D	R	O	P	E	R	K	N	I	O	B	L	O	O	D	S	L	E	V	H	E	E
K	Y	I	Z	B	A	T	S	A	L	I	C	Y	L	A	T	E	S	S	L	U	R	R	E	D	P
V	H	C	M	O	M	I	S	T	H	E	B	E	S	T	N	I	S	G	U	L	S	L	I	P	I
Q	P	I	G	I	W	A	T	E	R	F	A	L	L	S	L	I	P	U	P	O	O	D	L	E	N
B	E	T	A	A	D	R	E	N	E	R	G	I	C	A	N	T	A	G	O	N	I	S	T	S	E
B	J	Y	L	A	K	L	E	P	T	O	M	A	N	I	A	C	A	D	E	M	Y	C	A	R	S
U	C	A	L	C	I	U	M	C	H	A	N	N	E	L	B	L	O	C	K	E	R	S	X	C	V
X	D	N	H	T	N	E	E	R	C	S	Y	G	O	L	O	C	I	X	O	T	E	N	I	R	U

1. Lag of which treatments in a Toxic Alcohol case are pitfalls:
   _____ & _____.
2. A treatment pitfall in TCA treatment that causes:
   Seizures is _____
   Cardiac Arrest _____
3. Discontinuing NAC therapy in toxic APAP when subsequent APAP levels fall below the _____.
4. Lack of hyperventilating patients with exposure to _____.
5. Delay of WBI for large mg sustained release formulations of these medications:
   _____ & _____.
6. These drugs should not be given for cocaine related HTN & tachycardia:
   _____.
7. Patients exposed to CO should receive this treatment if within 24 hours if indicated: _____.
8. Patients that ingest Astemizole or Terfenidine will appear asymptomatic but can have this:
   _____
9. _____ should be used to monitor for methemoglobin in NTG overdoses.
10. This lab result often done in ED's for the OD pt. can over shadow assessment:
    _____
11. In Klonopin OD, most ED's shy away from this medication for treatment of agitation or sedation:
    _____
12. This drug, sometimes given for agitation in OD situations is not recommended as it may lower seizure threshold:
    _____
13. _____, _____, and _____ are sometimes overlooked during assessment of OD patient.

TEXT ANSWERS (*word search answers on page 8*):
1. folepizole, ethanol; 2. flumazenil, physostigmine; 3. nomogram; 4. salicylates; 5. beta blockers, calcium channel blockers; 6. beta adrenergic antagonists; 7. hyperbaric; 8. cardiotoxicity; 9. pulse oximetry; 10. urine toxicology screen; 11. benzodiazepines; 12. haldol; 13. pupils, bowel sounds, reflexes

SPI CORNER:
HOLIDAY POISONINGS

Continued from page 6

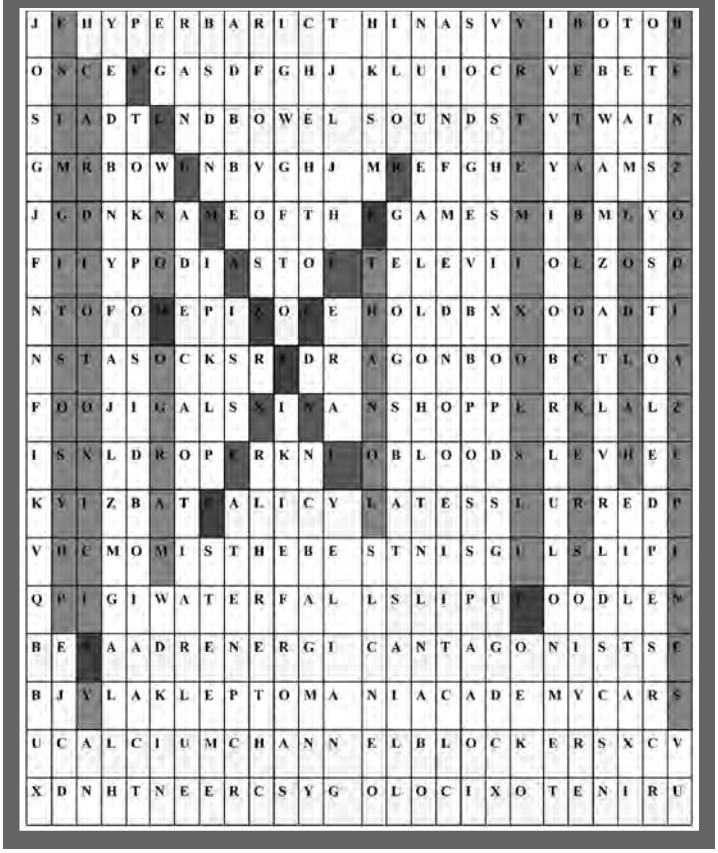
Christmas time also has some of these same hazards, along with some that are unique to it self.

- Holiday plants such as Holly, Mistletoe, and Amaryllis may result in symptoms of toxicity in relatively small ingestions. Home follow up with referral to an emergency room as needed is indicated for ingestions of these. Christmas trees are not considered toxic, but needles may cause mechanical injury if swallowed.
- Decorations are unlikely to cause toxicity except in rare cases and are mainly a choking hazard for children. Leaded paint on ornaments is unlikely to produce toxicity from a single small exposure. The fluid inside snow globes is non-toxic but, if a small leak occurs, bacterial contamination may result in symptoms similar to bacterial food poisoning. Angel hair is spun glass and may be irritating to skin, so thorough washing is indicated after handling.

Specialists in poison information need to be aware of the toxicity and management of exposures that are common at holiday times. Good history taking and assessment are essential, since callers may be more frazzled during this hectic and emotional season.

Have a happy and safe holiday season!

Word Search Answers



State University of New York
Upstate Medical University
Upstate NY Poison Center
750 East Adams Street
Syracuse, NY
13210