



January 2006

The NY State Poison Centers

TOXICOLOGY

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LETTER

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

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

Please call administrative telephone numbers for more information.

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

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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.

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Symptomatic Hypoglycemia

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

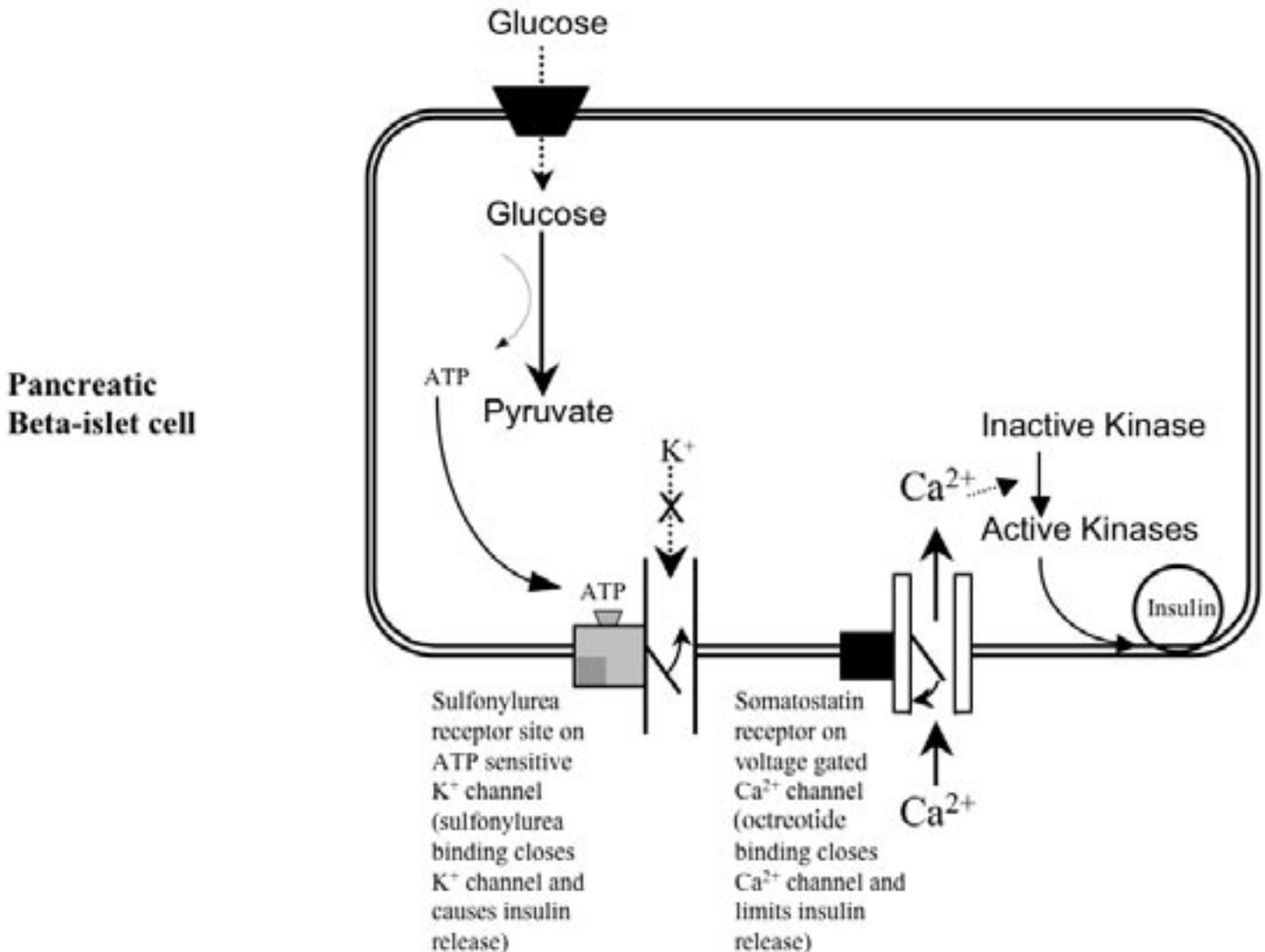
Her laboratory results drawn on presentation were as follows: Proinsulin: 366.0 pmol/L (range: 2.1-26.8), Insulin: 112 mIU/mL (range: 0.0-15.6), C-Peptide: 8.8 ng/mL (range: 1.1-4.6), Glipizide: 1 ng/mL (therapeutic: 100-1000 ng/mL). These values are consistent with glipizide ingestion because they confirm 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.

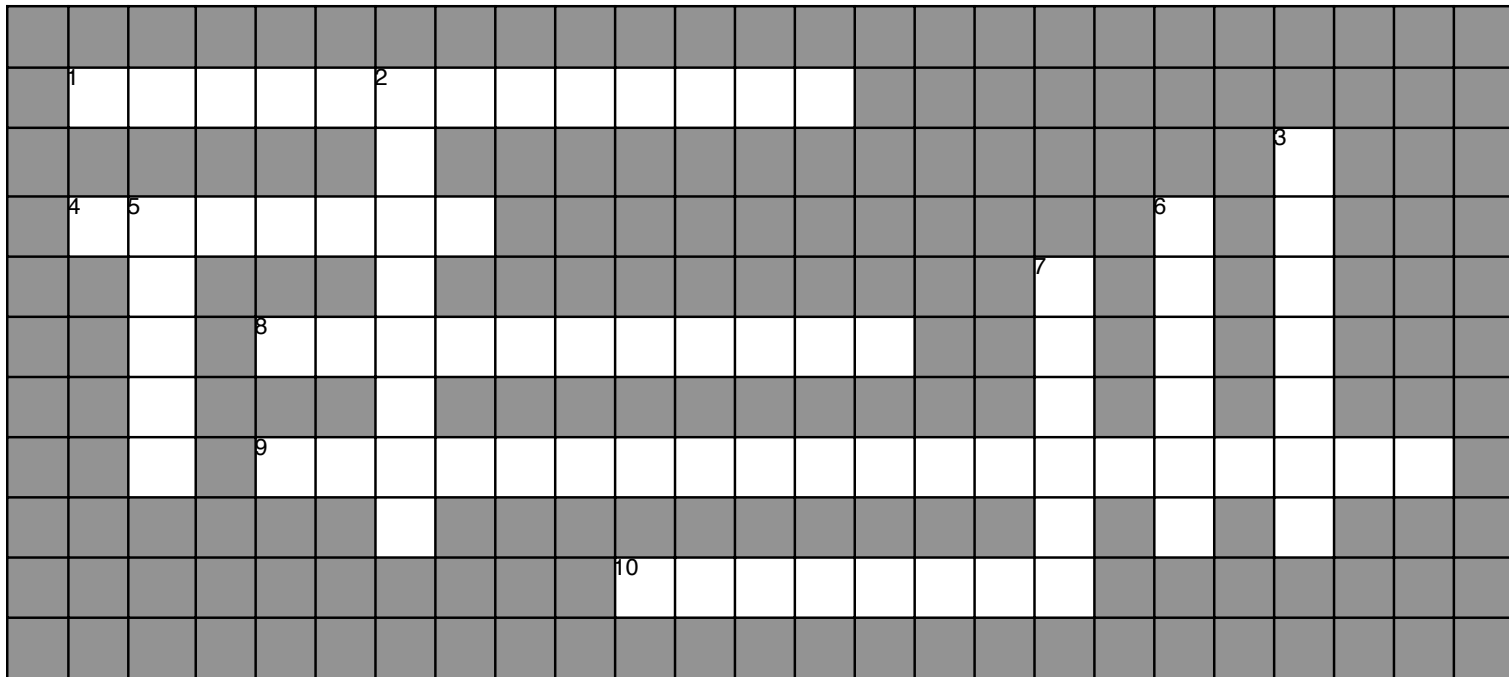
You can check specific products by contacting the Consumer Products Safety Commission product recalls at www.cpsc.gov.



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



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