



January 2005

The NY State Poison Centers

TOXICOLOGY

A Quarterly Publication • Vol. IX No. 5

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>

Finger Lakes Regional Poison & Drug Info Center (FL)

585.273.4155 • www.FingerLakesPoison.org

Central New York Poison Center (CNY)

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

Program Announcements • •

FL: Monthly conference: every 4 weeks on Thursdays starting Jan 27th (11 am to noon), and every 4 weeks on Tuesdays starting Feb 1st, 2005 (10 am-11 am).

CNY: Please mark your calendars for our Ninth Annual Toxicology Teaching Day to be held in the Fall of 2005. More information to come.

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

LI: January 27, 2005: Pediatric Toxicology
Howard Mofenson, MD

March 3, 2005: Herbal Toxicology
Ms. Elaine Yum, RPH,CSPI

March 30, 2005: Sports Toxicology
David Lee, MD

These conferences are available by telephone and broadband TV format from 12-2PM

Contact Tom Caraccio at Tcaracci@winthrop.org to register

Please call administrative telephone numbers for more information.

Tox Trivia • •

1. Anesthetic removed from the market in 1976 because of studies linking it to cancer in animals?
2. The presence of toxins in neonatal hair indicates an exposure in what trimester of pregnancy?
3. The only method of testing for anabolic steroid use accepted by the International Olympic Committee?

NYPC Tidbits • •

1. What is a common over the counter medication that can cause a false positive for PCP in a urine drug screen?
2. Toxic alcohol metabolized to formic acid?
3. Dermal post mortem finding after CO exposure?

Answers on page 6

Bicillin C-R (penicillin G benzathine and penicillin G procaine injectable suspension)

Bicillin L-A (penicillin G benzathine injectable suspension)

King Pharmaceuticals and FDA reminded health-care professionals of postmarketing reports of inappropriate use of Bicillin C-R to treat patients infected with syphilis. Bicillin L-A is the only currently approved penicillin G benzathine product indicated for the treatment of syphilis and Bicillin C-R should not be administered in place of Bicillin L-A. Administration of Bicillin C-R instead of Bicillin L-A in the treatment of syphilis may result in inadequate treatment.

In addition, a BLACK BOX WARNING has been added to the prescribing information of both products to emphasize that these products should only be administered by deep intramuscular injection. They are not intended for intravenous administration and inadvertent intravenous administration of penicillin G benzathine has been associated with cardiorespiratory arrest and death. *November 2004*

Depo-Provera (medroxyprogesterone acetate injectable suspension)

FDA and Pfizer notified healthcare professionals of the addition of a BOXED WARNING along with revisions to the WARNINGS, INDICATIONS AND USAGE, PRECAUTIONS and POSTMARKETING EXPERIENCE sections of the prescribing information to include information on the loss of significant bone mineral density. Depo-Provera Contraceptive Injection is indicated only for the prevention of pregnancy in women of child-bearing potential. Bone loss is greater with increasing duration of use and may not be completely reversible. Depo-Provera Contraceptive should be used as a long-term birth control method (eg, longer than 2 years) only if other birth control methods are inadequate. *November 2004*

Mifeprex (mifepristone)

Danco Laboratories and FDA notified healthcare professionals of revisions to the BOXED WARNING and WARNINGS sections, the MEDICATION GUIDE and PATIENT AGREEMENT of the Prescribing Information to describe serious and sometimes fatal infections and bleeding that may occur following the use of Mifeprex. *November 2004*

Humira (adalimumab)

FDA and Abbott Pharmaceuticals notified health-care professionals of revisions to the WARNINGS section of the prescribing information, indicated for the treatment of rheumatoid arthritis. These warnings

include serious infections with the combined use of Humira (adalimumab) and anakinra, hypersensitivity reactions, including anaphylaxis, and hematologic events, including pancytopenia and aplastic anemia. *November 2004*

Actra-Rx and Yilishen dietary supplements

The FDA warned consumers not to purchase or to consume Actra-Rx or Yilishen, two products promoted and offered for sale on Web sites as "dietary supplements" for treating erectile dysfunction and enhancing sexual performance for men. FDA testing of Actra-Rx found that the product contained undeclared prescription-strength sildenafil. An interaction between sildenafil and certain prescription drugs containing nitrates (such as nitroglycerin) or nitrates found in illicit substances (such as amyl nitrate) may cause a significant lowering of blood pressure to an unsafe level. Consumers who have taken Actra-Rx or Yilishen should stop taking it and consult with their health care providers regarding erectile dysfunction treatment. *November 02 2004*

Reminyl (galantamine hydrobromide)

FDA, Janssen Pharmaceutica Products, and Johnson & Johnson Pharmaceutical Research & Development notified healthcare professionals of reports of medication errors involving confusion between Reminyl, a drug approved for the treatment of mild to moderate dementia of the Alzheimer's type, and Amaryl (glimepiride), a product of Aventis Pharmaceuticals, indicated for the treatment of non-insulin dependent (Type 2) diabetes mellitus. These reports include instances in which Reminyl was prescribed but Amaryl was incorrectly dispensed and administered instead, leading to various adverse events including severe hypoglycemia and one death. *October 2004*

Public Health Advisory: Suicidality in Children and Adolescents Being Treated with Antidepressant Medications

The Food and Drug Administration issued a Public Health Advisory, asking manufacturers of all antidepressant drugs to revise the labeling for their products to include a boxed warning and expanded warning statements that alert health care providers to an increased risk of suicidality (suicidal thinking and behavior) in children and adolescents being treated with these agents, and additional information about the results of pediatric studies. FDA also informed these manufacturers that it has determined that a Patient Medication Guide (MedGuide), which will be

Continued on page 5

A Fatal Drug Interaction

Case Report:

Contributed By: S. Eliza Halcomb MD, Lewis Nelson MD. New York City Poison Control Center.

A 54-year-old man was brought into the emergency department complaining of crushing substernal chest pain after using cocaine earlier that morning. The pain was of sudden onset, lasting for three hours, aggravated by exertion and relieved by rest. He also complained of nausea and vomiting as well as recent three pillow orthopnea and paroxysmal nocturnal dyspnea. His past medical history was significant for hypertension. He denied taking any medications and had no known drug allergies. His social history was remarkable for a 30-pack year smoking habit and frequent cocaine use.

On examination, he was alert and oriented sitting up in bed. His blood pressure was 145/95 mmHg, heart rate was 115/min, breathing at 20/min and he was afebrile with a temperature of 96.8°F. His cardiovascular exam was notable for tachycardia and jugular venous distension. His lungs were clear to auscultation bilaterally, with no notable wheezes or crackles. His abdominal and neurologic exams were normal.

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

The symptoms described by this patient are concerning for an acute coronary syndrome such as unstable angina or myocardial infarction. The initial management, particularly in this patient experiencing subjective breathing difficulties, should include assurance of adequate gas exchange (airway and breathing) as well as circulation.

These issues each need to be addressed to minimize damage to ischemic cardiac muscle. The initial interventions in this case included placing the patient on oxygen, placing an intravenous catheter and placing the patient on a monitor. He then had an ECG done and labs sent.

What are the pharmacologic agents used to treat acute coronary syndromes?

All patients presenting with chest pain believed to be of cardiac origin should receive an aspirin and nitroglycerin, unless contraindicated. Aspirin has anti-platelet effects that prevent clot formation and nitroglycerin has vasodilatory effects that help increase blood flow to potentially ischemic myocardium. In addition, intra-

venous morphine alleviates pain, which reduces the patient's sympathetic tone and decreases the adverse hemodynamic effects of pain and dyspnea. Although improving blood flow to the heart is paramount, a critical additional intervention includes reducing the oxygen requirement of the heart. Beta-adrenergic antagonists alleviate the patient's tachycardia by preventing the binding of endogenous catecholamines on the cardiac β -1 adrenergic receptors. Blockade of these receptors has both negative inotropic and chronotropic effects leading to reduction of cardiac work and oxygen consumption as well as a reduction in the mean arterial blood pressure. Note that because there are β -2 receptors on the skeletal muscle vasculature, the use of non-selective β -adrenergic antagonists does not typically result in a precipitous fall in mean arterial blood pressure. That is, since stimulation at these receptors produces vasorelaxation, mild peripheral vasoconstriction may occur through their antagonism.

Are there any concerns about using the traditional pharmacologic agents in this setting?

This patient had used cocaine on the day of presentation. Cocaine is a centrally acting sympathomimetic agent. Its mechanism of action is to prevent the reuptake of norepinephrine and other biogenic amines at nerve endings, which, among other things, increases the outflow of activity via the peripheral sympathetic nerves. Alpha-adrenergic receptor stimulation is prominent from the peripherally-released norepinephrine in patients with high sympathetic tone, resulting in vasoconstriction and hypertension.

Given its central nervous system site of action, the most effective way to treat the clinical manifestations of cocaine is with sedation, typically with benzodiazepines. By decreasing central nervous system activity, there is a concomitant reduction in peripheral sympathetic outflow. If this does not produce sufficient hemodynamic control, vasodilators such as nitroprusside, or preferentially phentolamine, an α -adrenergic antagonists, may be useful.

There are major concerns about using β -adrenergic antagonists to reduce the heart rate or blood pressure

Continued on page 4

in patients with cocaine-related ischemia. Since cocaine causes α -mediated vasoconstriction, β -adrenergic antagonism may block β -2 mediated vasodilation. Thus, the concomitant use of β -adrenergic antagonists may result in life-threatening hypertension and associated complications as a result of “unopposed alpha” vasoconstriction. That is, since cocaine causes its peripheral hemodynamic effects through the release of norepinephrine from the sympathetic nervous system, and since norepinephrine has a potent α -adrenergic agonist effect, the use of non-selective (and probably all) β -adrenergic antagonists eliminate the small amount of β -2 mediated vasodilatation. Thus, the α -adrenergic effects remain and produce unopposed vasoconstriction. A 1990 study by Lange et al. found that administration of propranolol in the setting of low dose cocaine use resulted in increased coronary vascular resistance and a reduction in the diameter of the coronary artery. A 1993 study by Boehrer et al showed that labetalol administration in the setting of low dose cocaine use caused an increase in mean arterial blood pressure, no change in heart rate and a decrease in coronary artery area, and clearly demonstrated coronary artery vasoconstriction angiographically. That is, labetalol, despite its α -adrenergic antagonistic effects, is no better than propranolol.

Case Continuation

This patient’s pain was completely relieved with the administration of aspirin, however he remained tachycardic and hypertensive, which concerned the clinician due to the aforementioned increase in oxygen

Tox Trivia Answers • •

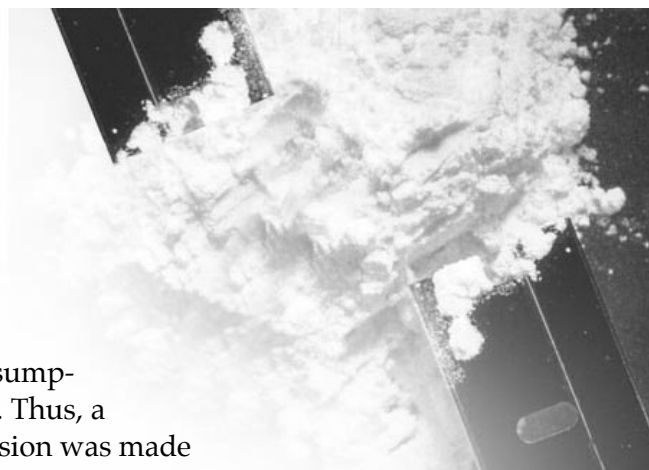
1. chloroform
2. Third
3. gas chromatography / mass spectrometry

NYPC Tidbits Answers • •

1. dextromethorphan
2. methanol
3. cherry red skin

Crossword Answers • •

Across: 1. Sodiumchloride 4. Elementalmercury 7. Tetrahydrolazine 9. Erythromycin 10. Methanol; **Down:** 2. Diphenhydramine 3. Dextromethorphan 5. Carbon-monoxide 6. Ethyleneglycol 8. Camphor



consumption. Thus, a decision was made to use benzodiazepines to treat his heart rate and blood pressure. However, this patient’s heart rate and blood pressure remained slightly elevated one hour after his arrival to the emergency department (about 6 hours after his cocaine use). A decision was made to administer intravenously a low dose (2.5 mg) of metoprolol. This lowered the systolic blood pressure to 125 mmHg and his heart rate dropped from 115 to 105. Another 2.5 mg metoprolol was administered minutes later, after which the patient immediately complained of severe chest pain, vomited and collapsed. CPR was commenced with no return of spontaneous circulation.

This was an unfortunate case in that the physician felt that since the patient had used cocaine 6 hours prior to arrival, it was probably safe to treat with a β -adrenergic antagonist. However, it must be noted that although cocaine is rapidly eliminated from the body through metabolism, it has several vasoactive metabolites that may be active for at least a day postexposure. Therefore, the use of β -adrenergic antagonists cannot be recommended in patients with symptoms and signs of coronary ischemia in the setting of recent cocaine use. When it is safe to use β -adrenergic antagonists remains a matter of debate. However, give the limited data that early β -blockade is better than subsequent administration it seems prudent to avoid their use in the first 24 hours post-cocaine use.

Select References.

- Boehrer J. et al. Influence of labetalol on cocaine-induced coronary vasoconstriction in humans. *Am J Med* 1993;94:608-610.
- Catravas JD, Waters IW. Acute cocaine intoxication in the conscious dog: studies on the mechanism of lethality. *J Pharmacol Exp Ther* 1981;217:350-356.
- Lange RA et al. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med* 1990;112:897-903

SPI CORNER TOPIC: **TOXIC MOLD**

Contributed by: Margo M. Spain RN, CSPI, Mary Halsey-Claps RN, CSPI, Central New York Poison Center, Syracuse, NY

Summer is over, windows are closed, the poison centers call volume regarding toxic molds is increasing. After sifting through the volumes of information referring to molds, we felt some information needed clarification.

What is mold?

Mold is everywhere. It has characteristics of plants and animals. Mold is a visible colony of fungi. Most fungi are saprophytes which breakdown decaying materials then absorb the decayed material as nutrition. They serve a critical role in the ecology of decaying materials. Molds grow anywhere there is sufficient moisture and nutrient source indoor or outdoor environments over a broad spectrum of temperatures. Dirt, dust, wood, paper, paint, and insulation are common materials of nutrition combined with moisture. Mold in itself is not a problem when the source is in the normal interchange of outside and indoor air. When the balance is off and increased moisture rises to an ideal environment for amplification of mold growth which promote as a byproduct mycotoxins or bacterial volatile organic compounds.

Three common types of molds are zygomycetes, ascomycetes and basidiomycetes that contaminate buildings. The most common indoor molds are Cladosporium, Penicillium, Aspergillus, Stachybotrys chartarum, and Alternaria. The Stachybotrys atra and the Aspergillus versicolor are known to produce potent toxins under certain circumstances. Stachybotrys chartarum and Aspergillus prefer cellulose on wall board.

Health Effects

Mold exposure does not always present a health problem, however some people are sensitive and exposure can result in infections, hypersensitivity, irritant or toxic reactions. Hypersensitive reactions can go on to cause allergic rhinitis, asthma or hypersensitivity pneumonitis. Although certain mycotoxins are known to be responsible for health effects, little information is available on others.

Two conditions involve a more intense immunologic response to fungi: allergic bronchopulmonary aspergillus (ABPA) and allergic fungus sinusitis (AFS). ABPA occurs in patients with underlying asthma and cystic fibrosis who develop Aspergillus colonization of the airway.

In December 1994 and January 1997, a cluster of 10* infants from Cleveland, Ohio, with Acute Idio-

pathic Pulmonary Hemorrhage (AIPH) also referred to as Pulmonary Hemosiderosis were found to reside in the same postal tracts and had one or more hemorrhagic episodes, resulting in one death. Preliminary results of a CDC case-control study indicated that hemorrhage was associated with 1) major household water damage during the 6 months before illness and 2) increased levels of measurable household fungi, including the toxin-producing mold Stachybotrys chartarum.

To date, a possible association between Acute Idiopathic Pulmonary Hemorrhage (AIPH) among infants and the stachybotrys chartarum has not been established. The CDC will continue to investigate and consider possible associations between AIPH and mycotoxin exposure.

Testing

Generally, it is not necessary to identify the species of mold growing in a residence.

The CDC does not recommend routine sampling for molds. Reliable sampling for mold can be expensive and standards for judging what is and what is not an acceptable or tolerable quantity of mold has not been established. In certain instances, such as cases where health concerns are an issue, litigation is involved, or the source(s) of the contamination is unclear, sampling may be considered as part of a building evaluation.

The Health Department, although it will not do testing, will send in a county sanitation representative to observe the mold and give recommendations. They will follow up with the landlord and perform a home inspection to ensure that the mold situation has been corrected.

Remediation of Molds

If mold is visible, then it should be remediated, regardless of what species is present. If the building smells moldy, but you cannot see the source you should suspect a hidden mold problem. Moisture control is the key to mold control. Mold will often grow in damp or wet areas indoors. Common sites include bathroom tiles, under water damaged floors and carpeting, behind wallpaper and paneling and

Continued on page 6

FDA Safety Summaries

Continued from page 2

given to patients receiving the drugs to advise them of the risk and precautions that can be taken, is appropriate for these drug products. October 2004

Remicade (infliximab)

FDA and Centocor notified healthcare professionals of revisions to the WARNINGS and ADVERSE REACTIONS sections of the prescribing information for Remicade, indicated for the treatment of rheumatoid arthritis and Crohn's disease. In controlled studies of all TNF-blocking agents, including Remicade, more cases of lymphoma have been observed among patients receiving the agents than among control group patients. Malignancies have also been observed in open-label, uncontrolled clinical studies at a rate several-fold higher than expected in the general population. Patients with Crohn's disease or rheumatoid arthritis, particularly patients with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at a higher risk (up to several fold) than the general population for the development of lymphoma. FDA has recommended a warning concerning malignancy be added to the labeling for all therapeutic agents that block TNF. October 2004

Levoxyll (levothyroxine sodium)

FDA and King Pharmaceuticals notified healthcare professionals of revisions to the PRECAUTIONS, ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections of labeling, describing reports of choking, gagging, tablets stuck in throat and dysphagia while taking Levoxyll. These reports have

predominately occurred when Levoxyll tablets were not taken with water. It is recommended that Levoxyll tablets be taken with a full glass of water. September 1,7 2004

Zometa (zoledronic acid) Injection

FDA and Novartis notified healthcare professionals of revisions the PRECAUTIONS and ADVERSE REACTIONS sections of labeling, describing spontaneous reports of osteonecrosis of the jaw mainly in cancer patients, who have received bisphosphonates as a component of their therapy. A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene). September 24, 2004

Vioxx (rofecoxib)

Merck & Co., Inc. announced a voluntary withdrawal of Vioxx (rofecoxib) from the U.S. and worldwide market due to safety concerns of an increased risk of cardiovascular events (including heart attack and stroke) in patients on Vioxx. Vioxx is a prescription COX-2 selective, non-steroidal anti-inflammatory drug (NSAID) that was approved by FDA in May 1999 for the relief of the signs and symptoms of osteoarthritis, for the management of acute pain in adults, and for the treatment of menstrual symptoms, and was later approved for the relief of the signs and symptoms of rheumatoid arthritis in adults and children. September 30, 2004

SPI CORNER TOPIC: TOXIC MOLD

Continued from page 5

basement walls.

The Health Department and the CDC recommend that in most cases mold can be removed by a thorough cleaning with a detergent, bleach and water solution. If there is an extensive amount of mold, professional remediation may be required. Persons cleaning mold should wear protective clothing, rubber gloves, eye protection, and a N95 dust mask or respirator. The area should be well ventilated.

Public awareness has increased regarding toxic molds. Litigation and proposed legislation have been put forth in an attempt to bring increased action to remedy the health risk and property damage caused by this national problem.

References:

March 10, 2000: MMWR Update: Pulmonary Hemorrhage/Hemosiderosis Among infants Cleveland, Ohio, 1993-1996

Guidance for Clinicians on the recognition and management of health effects Related to Mold Exposure and Moisture Indoors - September 30, 2004

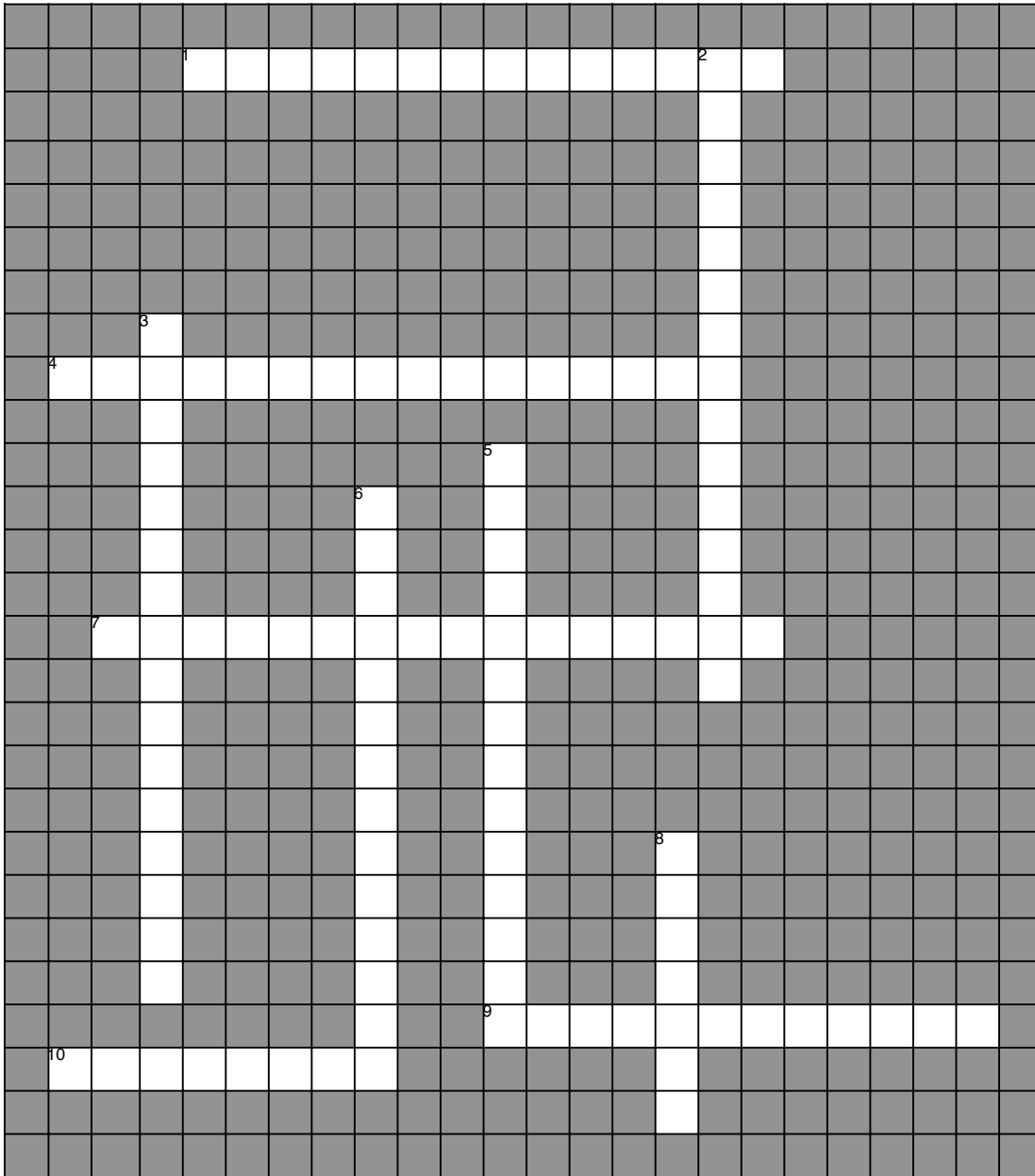
Report to the CDC Working Group on Pulmonary hemorrhage/Hemosiderosis- June 17, 1999

CDC/NCID Division of Bacterial and Mycotoxic Diseases: Fungal Diseases

TOXICOLOGY CROSSWORD

WINTER TOXINS

Contributed by: Laurie Piwinski, RN, CSPI Central New York Poison Control Center, Syracuse, NY



Across

1. Ingredient in ice-melting crystals that may cause initial vomiting when ingested
4. Substance that is non toxic when swallowed if a thermometer breaks in the mouth
7. Ingredient in ophthalmic and nasal preparations that has a clonidine-like effect after ingestion
9. Antibiotic with many drug interactions due to it's ability to inhibit CYP 3A4
10. Deadly toxin in windshield washer fluid

Down

2. Over the counter allergy medication that may cause lilliputian hallucinations in overdose
3. Common over the counter medication abused by teens
5. Odorless, tasteless gas; #1 poisoning killer
6. Ingredient in radiator antifreeze responsible for metabolic acidosis, renal failure and death in poisonings
8. Toxin in liniments and vaporizer additives that can cause seizures after ingestion



GNV Poison Center
750 East Adams Street
Syracuse, NY
13210