

Central
New York
Regional
Poison
Control
Center

The CNYPCCC

January 2000

Toxicology Letter

Vol. V No. 1

A Quarterly Publication

SCHEDULED EVENTS:

Emergency Medicine Grand Rounds
Marley Education Center: Sulzle Auditorium
Third Friday of the Month, 11:00 AM

January 21, 2000
February 18, 2000
March 17, 2000

Toxicology Case Conference
CNYPCCC, 550 E Genesee Street
Poison Center Conference Room
Every Thursday 10:00 AM – 11:00 AM

PROGRAM ANNOUNCEMENT:

We hope all enjoyed our Third Annual Toxicology Teaching Day. Handout materials are available for those desiring and extra copy or those who could not be with us. Please call 464-7078 for more information.

CNYPCCC TIDBITS:

Medication Errors: Describe what is wrong with each order

1. Propranolol 1.0 mg intravenously
2. 1 vial of esmolol intravenously
3. 4-MP 750 mg stat

TOX TRIVIA:

1. The drug can produce cyanide in select patients
2. Which toxic alcohol results in ketosis without producing an acidosis
3. What is the antidote for hydrofluoric acid burns

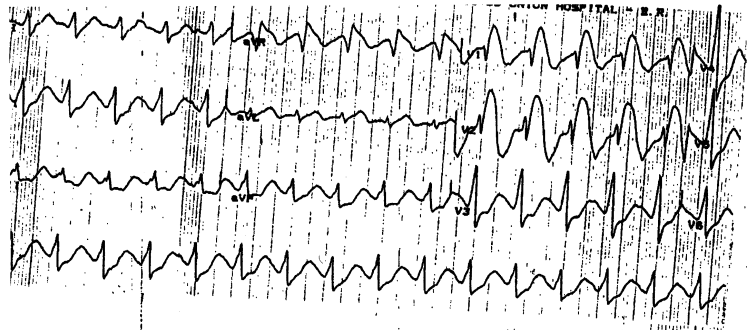
Case History

Contributed by: Christine M. Stork, Pharm.D., ABAT

WHERE ARE THE LIFE-THREATS?

Case:

A 45 year old female is brought into the emergency department after trying to harm herself using medications. She is initially alert and oriented with a blood pressure of 130/70 mmHg, heart rate of 115/minute, respiratory rate of 15/minute and temperature of 37 C. Over the next 30 minutes she becomes lethargic and is not responsive to deep pain. She experiences a 20 second tonic clonic seizure. Upon re-assessment, the patient is found to have a blood pressure of 120/p, a heart rate of 140/minute, respiratory rate of 12/minute and temperature of 37.9 C. Physical examination is significant for 7 mm pupils, dry mucous membranes, normal chest and heart examination, and absent bowel sounds. An ECG reveals the following:



What are the toxins that are likely to result in death in 1999?

The last report of data from the American Association of Poison Control Centers (AAPCC) lists tricyclic antidepressants (TCA) (98) as the leading cause of death in the United States. TCAs were followed by acetaminophen (34 alone /87 with others [opioids]), salicylates (36), opioids (57), cocaine (43), digoxin (19), carbon monoxide (31), and calcium channel antagonists (61). Carbon monoxide is still a serious risk for mortality as reported through the medical examiners office. Cases reported to the AAPCC are a gross underestimation of the true incidence of exposure due to the inherent nature of a voluntary reporting system.

WHERE ARE THE LIFE-THREATS?

(CONT.)

What toxin has this patient likely been exposed to?

This patient is experiencing typical manifestations of anticholinergic (antimuscarinic) toxicity. Antagonists at post-ganglionic parasympathetic receptors typically cause a constellation of physical findings including mydriasis, dry and flushed skin, dry mucous membranes, decreased bowel sounds and urinary retention. Vital signs are significant for tachycardia and increased temperature. Mental status changes are variable and include depression, hallucinations and seizures. Typical anticholinergic drugs include atropine, scopolamine, diphenhydramine, chlorpheniramine, hydroxyzine and meclizine. This patient is also experiencing a supraventricular increased QRS complex duration dysrhythmia. The most likely toxin causing these problems concurrently is the tricyclic antidepressants.

How do tricyclic antidepressants cause toxicity?

TCAs include imipramine (Tofranil®), amitriptyline (Elavil®), desipramine (Norpramin®), nortriptyline (Pamelor®) and doxepin (Sinequan®). The pharmacologic mechanisms attributed to TCAs are many and include; inhibition of muscarinic acetylcholine receptors (anticholinergic), inhibition of fast sodium channels (Type 1A antidysrhythmic effect), inhibition of gamma amino butyric acid (GABA), inhibition of post synaptic alpha adrenergic receptors, and inhibition of the re-uptake of catecholamines. Each of these mechanisms contribute to this patient's overall clinical presentation of anticholinergic excess with a wide QRS complex duration concurrent with seizure activity. In addition, patients may experience hypotension due to both alpha adrenergic blockade and long term depletion of presynaptic stores of catecholamines from reuptake inhibition.

Is there a way that I can predict who has been exposed to a tricyclic antidepressant or who will become sick?

Many times patients appear well initially and then go on to rapidly decompensate. The mean time from toxin exposure to significant clinical toxicity is 1.5 hours. In the initial evaluation, it is useful to obtain an ECG both to evaluate the patient for tricyclic antidepressant exposure, and to evaluate for the risk of toxicity. In acutely overdosed patients, a rightward axis deviation of the terminal 40 msec of the QRS complex (patients having a r wave in AVR) is a sensitive and specific marker for exposure to a tricyclic. These patients may not experience toxicity, but should be monitored carefully. QRS complex duration predicts the risk for seizures and dysrhythmias, which are the two serious effects seen after TCA poisoning. If the QRS complex duration in any

of the limb leads exceeds 100 msec the patient is at risk (approximately 1/3) for seizures and if the duration exceeds 160 msec the patient is at risk (approximately 1/3) for ventricular dysrhythmias. Patients who do not experience significant QRS complex duration widening by 6 hours after exposure do not go on to experience subsequent toxicity. In addition, although TCA levels are sometimes useful to monitor therapeutic benefit, they do not correlate with toxicity and should not be used to monitor patients.

Do tricyclic antidepressant poisoned patients benefit from gastrointestinal decontamination?

Early aggressive gastrointestinal decontamination using orogastric lavage may provide benefit in reducing the milligram amount ingested and therefore prevent lethality. In addition, because tricyclic antidepressants are anticholinergic with an early onset of toxicity, drug may be available in the stomach for a longer period of time than a generic toxin. Activated charcoal does not adhere to tricyclic antidepressants and should be used, even after trivial exposures. Multiple doses of activated charcoal may be of benefit for large milligram amounts ingested or to interrupt enterohepatic recirculation that occurs with many TCAs.

What should be done if a patient presents or develops with a widened QRS complex duration?

Patients experiencing a widened QRS complex duration should receive alkalinization and sodium administration. Alkalinization of the patient decreases the affinity of the TCA for the myocardium. Sodium administration directly competes with the fast sodium channel blockade to increase sodium conductance. Both therapies work effectively alone, but both together may provide more therapeutic benefit. 1-2 mEq/kg of sodium bicarbonate is used as a loading dose followed by either further boluses or an intravenous infusion of 3 ampules (132-150 mEq of sodium) in 1 liter of D5W infused at 1.5-2 times maintenance. Arterial pH should be monitored and maintained between 7.45-7.55 and the patient should be closely monitored for fluid and pulmonary status. The endpoint of therapy is narrowing of the QRS complex duration.

Is there any specific treatment for seizures caused by tricyclic antidepressants?

Seizures caused by TCAs are usually short, generalized, and do not require treatment. Benzodiazepines are useful if treatment is required, followed by barbiturates, and finally general anesthesia for refractory cases. Phenytoin is not effective for TCA induced seizure activity and may actually be harmful. In

WHERE ARE THE LIFE-THREATS? (CONT.)

animal models, the administration of phenytoin to TCA poisoned animals resulted in an increase in ventricular dysrhythmias. Sodium bicarbonate may not alleviate seizures caused by tricyclic antidepressants. However, it provides a buffer for the resultant acidosis which left untreated would enable increased binding of the TCA at the level of the myocardium. Of note, flumazenil can abruptly cause seizures if given to a patient who has ingested a TCA and therefore, should not be considered in these patients.

Is there any specific treatment for dysrhythmias caused by tricyclic antidepressants?

Sodium and bicarbonate therapy should be the treatment of choice for dysrhythmias caused by tricyclic antidepressants. Antidysrhythmics that can further widen the QRS complex duration should be avoided including: IA antidysrhythmics (i.e. quinidine, procainamide), 1C antidysrhythmics (i.e. flecainide, encainide), and class III antidysrhythmics (i.e. sotalol). Lidocaine is safely used in these patients. Of note, physostigmine once thought to be an antidote for tricyclic antidepressant poisoning has resulted in cases of acute asystole. Therefore, its use is contraindicated in these patients.

Patient follow-up:

The patient receives 2 mEq/kg of sodium bicarbonate and is placed on a sodium bicarbonate drip. The QRS complex duration is narrowed to 120 msec. and the patient receives orogastric lavage and a dose of activated charcoal. After 6 hours the patient is found to have a blood pressure of 70/p. An initial trial of fluids followed by dopamine at 20 mcg/minute have produced no therapeutic effect.

Why is this patient not responding to our therapeutic gesture and is there alternative treatment available?

TCAs inhibit the re-uptake of catecholamines, eventually depleting the presynaptic stores. As dopamine initially works indirectly by causing the release of

catecholamines, it is unreliable in this population. Direct acting pressors that increase alpha-adrenergic activity such as norepinephrine, or ephedrine should be used.

How long do we expect this patient to experience toxicity?

Patients not experiencing toxicity from TCAs are free from developing toxicity after 6 hours. However, once toxic symptoms are present, they can persist for much longer than can be estimated from a therapeutic half-life. This is due to several factors. Absorption is slowed due to increased gastrointestinal tract burden influencing solubility in conjunction with anticholinergic effects and elimination is altered due to the large amount ingested.

Are there any experimental or anecdotal treatments for tricyclic antidepressant poisoning?

In severely poisoned hypotensive patients, intraaortic balloon pumps and cardiopulmonary bypass have been used. Also, in animal models using large doses of hypertonic sodium compared with sodium bicarbonate, it appears that sodium was more beneficial. Lastly, antibodies to tricyclic antidepressants are currently being formulated and tested. The main limitation thus far is the dose required to produce a therapeutic effect.

Select References:

Litovitz TL, Klein-Schwartz W, Carvati EM et al. 1998 Annual report of the American Association of Poison Control Centers toxic exposure surveillance system. *Am J Emerg Med* 1999;17:435-487.

Neimann JT, Bessen HA, Rothstein RJ et al. Electrocardiographic criteria for tricyclic antidepressant cardiotoxicity. *Am J Cardiol* 1986;57:1154-1159.

Boehnert M, Lovejoy FH Jr. Value of the QRS duration versus the serum drug level in predicting seizures and ventricular arrhythmias after an acute overdose of tricyclic antidepressants. *N Engl J Med* 1985;313:474-479.

Buchman AL, Daur J, Geiderman J. The use of vasoactive agents in the treatment of refractory hypotension seen in tricyclic antidepressant overdose. *J Clin Psychopharmacol* 1990;10:409-413.

Sasyniuk BI, Jhamandas V, Valois M. Experimental amitriptyline intoxication: Treatment of cardiac toxicity with sodium bicarbonate. *Ann Emerg Med* 1986;15:1052-1059.

CNYPCC Tidbits answers

1. 0 after a decimal place can be misread (instead of 1, 10)
2. 1 vial can contain 2500 mg instead of the intended 100 mg
3. 4-MP (abbreviation), can be misread as 4-mercaptopurine (chemotherapeutic agent) or 4-methylpyrasole (toxic alcohol antidote)

Tox Trivia answers

1. Sodium Nitroprusside
2. Isopropyl (rubbing) alcohol
3. Calcium or magnesium

THE "SPI" CORNER – TOPIC: NAACT 99 NEWS

Contributed by: Marvleen Hollenbeck, RN, CSPI

Two of the Specialists in Poison Information from the CNY PCC attended The North American Congress of Clinical Toxicology 99 meeting held in La Jolla, CA. New information was presented and current practice issues were discussed with poison specialists from around the country.

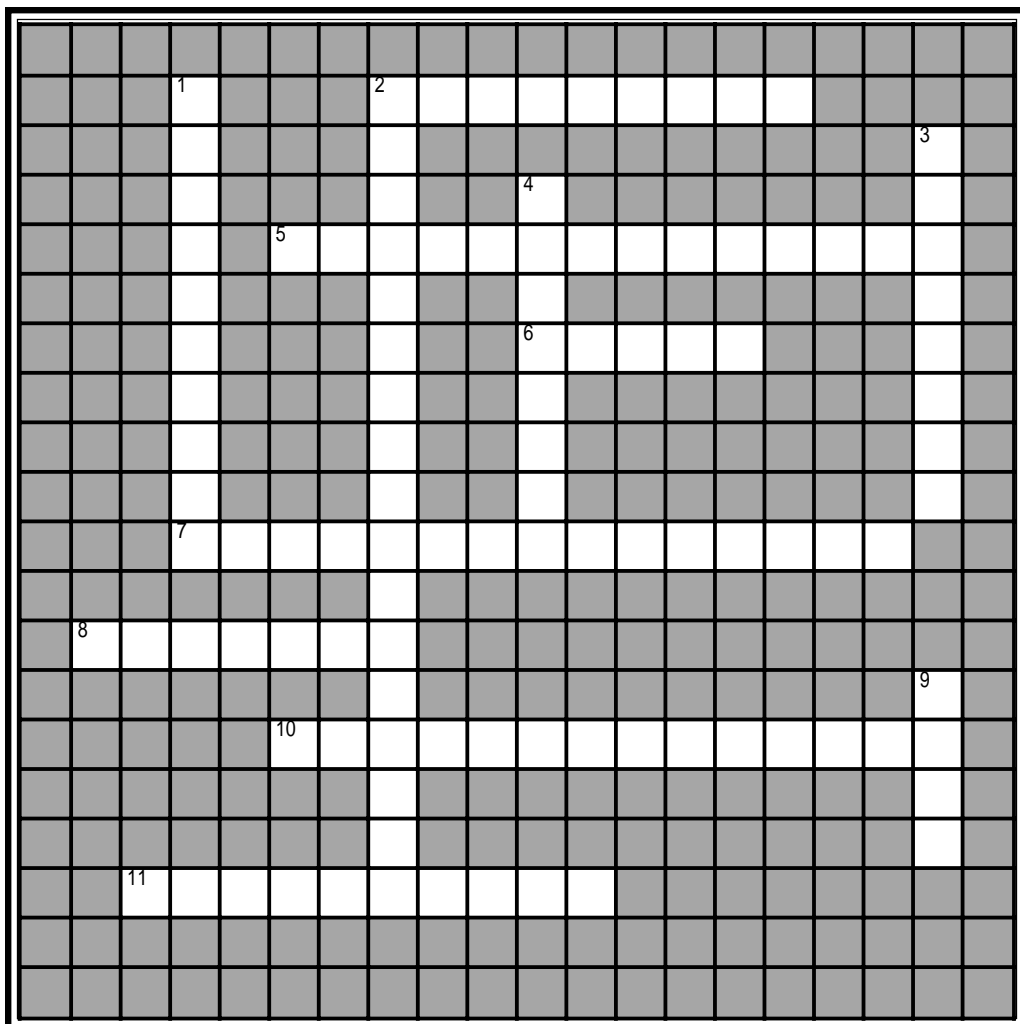
A symposium on "Anabolic-Androgenic Steroids and other Performance Drugs" was presented by Charles Yesalis, Scd. He emphasized that these drugs have been used for thousands of years and in fact, ancient Greeks used sesame seeds to enhance performance. The use of anabolic-androgenic steroids today is blamed on society's fixation on physical appearance and winning performances. Unfortunately, the extent of their use in the athletic community is often reported as anecdotal and not scientifically documented. This has impeded the development of effective drug abuse programs.

Another symposium entitled "Bites & Stings and Natural Things" included a lecture on "Necrotic Arachnidism" presented by Ronald Sherman, MD. He discussed the two venomous spiders: *Latrodectus mactans* (the Widow

spider) and *Loxosceles reclusa* (the Violin spider) . Although these two spiders are not native to our area, we occasionally see bites in our area due to increased availability of transport.

Latrodectus bites present with minimal erythema surrounding the wound and dull aching muscular pain radiating from the bite. The venom of this spider, alpha latrotoxin, is neurotoxic causing the release of neurotransmitters, resulting in their depletion, with the consequences of pre-synaptic blockade. Systemic effects include muscle spasms and pain, nausea and vomiting, and diaphoresis. Treatment includes analgesics, benzodiazepines, calcium gluconate ,and rarely, antivenin.

The other genus that is problematic in North America is *Loxosceles* whose venom is cytotoxic. Sphingomyelinase D causes actual tissue necrosis and red cell lysis. The bite is initially painless but becomes painful within hours. Within 1-7 days, necrosis at the site of the bite, (necrotic arachnidism) can occur. Treatment includes meticulous wound care, dapson e if started early, and ruling out other treatable causes.



HOLIDAY HAZARDS

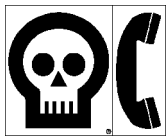
CLUES:
ACROSS

- 2. Pink berries and altered mental status
- 5. Woods lamp diagnosis
- 6. Plant causing GI upset
- 7. Cause of Rudolph's big eyes and red nose
- 8. New Years morning and hypoglycemia in children
- 10. Treatment is HBO
- 11. Non-poisonous holiday plant

DOWN

- 1. Bacteria found in show globes
- 2. Bubble light ingredient causing CO poisoning
- 3. Jerusalem cherry toxin
- 4. Blinding toxin
- 9. Antique ornament toxin

Across: 2. Mistletoe, 5. Ethylene glycol, 6. Holly, 7. Anticholinergic, 8. Ethanol, 10. Carbon monoxide, 11. Poinsettia
Down: 1. Salmonella, 2. Methylenechloride, 3. Solanine, 4. Methanol, 9. Lead



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April, 2000

Toxicology Letter

Vol. V No. 2

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SCHEDULED EVENTS:

Emergency Medicine Grand Rounds

NEW LOCATION & DAY:

Health Sciences Library Room 318

Second Wednesday of the Month, 11:00 AM

April 12; May 10; and June 14, 2000

Toxicology Case Conference

CNYPC, 550 E Genesee Street

Poison Center Conference Room

Every Thursday 10:00 AM – 11:00 AM

and every third Thursday 1 PM to 2 PM

PROGRAM ANNOUNCEMENT:

Please mark your calendars now and plan to attend our Fourth Annual Toxicology Teaching Day. We are planning an exciting line-up of lectures and workshops as well. The date is Wednesday November 1, 2000. A flyer will be coming shortly. Please call 464-7078 for more information.

CNYPC TIDBITS:

Match the toxin with the antidote:

- | | |
|-----------------------------|-----------------------|
| 1. ethylene glycol | a. sodium nitrite |
| 2. cyanide | b. sodium bicarbonate |
| 3. chloral hydrate | c. propranolol |
| 4. tricyclic antidepressant | d. ethanol |

TOX TRIVIA:

1. Which live species is not reported to contain a toxin? (snails, snakes, spiders, squirrels, birds)
2. Which is not a source of carbon monoxide? (furniture stripper, furnace, car, household iron)
3. True/False: Preformed toxin ingestion of botulinum is responsible for the majority of toxicity in infants.

Case History

Contributed by: Jennifer Falchek, Pharm.D. Candidate, Christine M. Stork, Pharm.D., ABAT

HYPOGLYCEMIC POISONING

Case:

A 75 year old male ingests all of his oral hypoglycemics in a suicide attempt. After 45 minutes, and in Emergency Care, he is alert and oriented with a heart rate of 75/minute, blood pressure of 150/85 mm Hg, respiratory rate of 14/minute, and temperature of 37 C (orally). Further history reveals that the patient is missing metformin (Glucophage) tablets.

What is the therapeutic role of metformin?

Metformin (Glucophage) is a biguanide oral hypoglycemic that exhibits antidiabetic effects through several pharmacologic mechanisms. Metformin enhances peripheral muscle glucose uptake, inhibits glucose release from the liver, and decreases intestinal glucose absorption. Metformin is considered most commonly as second line therapy and is therapeutically used in conjunction with another antidiabetic pharmaceutical.

Another antidiabetic of the biguanide class, phenformin was removed from the US market in 1976 due to a high risk of lactic acidosis (64 cases/100,000 patient years). This is due to the ability of phenformin to inhibit mitochondrial lactate utilization in addition to the pharmacologic effects noted for metformin. Phenformin cases of lactic acidosis may still occur in the US when patients receive medications from other countries. In particular, metformin is still available in Canada, Europe, and South America.

Metformin undergoes little mitochondrial binding. Lactic acidosis is seen, however, in approximately 3 cases/100,000 patient years. The mechanism thought related to metformin induced lactic acidosis includes decreased gluconeogenesis from alanine, pyruvate, and lactate leading to lactate accumulation. The risk of metformin associated lactic acidosis is increased with concurrent renal insufficiency and therefore the drug should not be used in these patients.

What are the consequences of metformin in the acute overdose setting?

There are few large case series detailing acute overdoses of metformin. Small case series suggest a risk of lactic acidosis

HYPOGLYCEMIC POISONING (CONT.)

without hypoglycemia. When lactic acidosis occurs in patients using therapeutic doses of metformin, it is considered life-threatening because reported case series demonstrate a death rate of approximately 50%. It is unclear how this finding should be extrapolated to the acute overdose setting. Hypoglycemia was only seen in patients with concurrent ingestions of insulin or sulfonylureas. Other symptoms reported in scant case reports include lethargy and disseminated intravascular coagulation (DIC). Patients who are not diabetic presented with symptoms of GI complaints, headache, and dizziness. A single case series of children with reports of accidental metformin exposure found no significant health risk of hypoglycemia and no evidence of lactic acidosis.

What other antidiabetic is this patient likely to have access to?

As metformin is a second line agent in the treatment of diabetes, it is likely that this patient has access to other commercially available antidiabetics, most of which are considered direct hypoglycemics. A list of currently available antidiabetic agents is seen on Table-1. A unique plant source of hypoglycemia is the Ackee fruit that is eaten in Jamaica. It has been reported to cause Jamaican vomiting illness when the unripe fruit, containing excess concentrations of the toxin, hypoglycin A, is consumed.

What are the manifestations of sulfonylurea overdose? Are there any patients at particular risk?

The sulfonylureas stimulate insulin release from pancreatic β -islet cells, reduce glycogenolysis, and increase insulin receptor sensitivity. The sulfonylureas, unlike the biguanides, lower blood glucose in normal patients. Children are very susceptible to sulfonylureas. There are case reports and retrospective case series of a single tablet causing hypoglycemia and although not confirmed in prospective case series, the onset of hypoglycemia in these children was reported to be substantially delayed.

Is there any way to tell whether this patient administered insulin?

The physical examination of a patient injecting insulin can be normal or may reveal a erythematous, boggy, hemorrhagic, and painful site.

The injection site can serve as depot for continuous insulin release. In addition, measured insulin levels should be elevated in the presence of hypoglycemia. C-peptide levels can be used as a quantitative marker to differentiate between endogenous insulin over production or release because unlike exogenous insulin, endogenous insulin is a proinsulin, cleaved to form insulin plus C-peptide. Another technique for determining the use of exogenous insulin is the presence of insulin binding antibodies, generally only present in patients using exogenous insulin.

What about the newer drugs? Are the thiolidinediones such as troglitazone, piaglitazone, and rosiglitazone toxic?

There is little information regarding overdose with the thiolidinediones. Overdose information is derived from adverse effects at therapeutic levels. Although infrequently reported, hypoglycemia can occur, especially when used in a poly-drug regimen. Reports of hepatotoxicity occur after therapeutic troglitazone therapy, but long-term studies especially on the recently released agents are lacking.

How long do we need to monitor this patient?

Due to the risk of poly-drug regimens and the lack of information regarding acute metformin overdose in adults, this patient should be monitored for 24 hours even if asymptomatic.

Are there any special antidotes we can use?

Glucose is the mainstay of therapy for hypoglycemia. It can be administered intravenously then orally when food is tolerated. Intravenous glucose should be given at a rate to keep the patient euglycemic, in order to prevent further insulin release and subsequent hypoglycemia. Regulators of insulin secretion that are available in cases not responding to caloric increases include diazoxide (Hyperstat[®]) and octreotide (Sandostatin[®]). Diazoxide directly inhibits insulin secretion by opening K_{ATP} channels. Because of adverse effects of sodium retention and hypotension and increased effectiveness with octreotide in simulated overdose models, octreotide is considered the insulin modular of choice. Octreotide inhibits glucose-stimulated β -cell insulin release through a G coupled protein.

HYPOGLYCEMIC POISONING (CONT.)**Table-1 Currently Available Antidiabetic Drugs**

CLASS	GENERIC	BRAND	INSULINS:	
			TYPE	BRAND NAME
Sulfonylureas	acetoexamide	Dymelor®	Short-acting very short-acting regular Intermediate-acting NPH Lente NPH/Regular mixtures Long-acting Ultralente	Humalog® Regular Iletin I & II® Humulin R® Novolin R® NPH Iletin I® Humulin N® Novolin N® Lentin Iletin I & II® Humulin L® Novolin L® Humulin 70/30® Humulin 50/50® Novolin 70/30® Humulin U®
	chlorpropamide	Diabinese®		
	tolazamide	Tolinase®		
	tolbutamide	Orinase®		
	glimepiride	Amaryl®		
	glipizide	Glucotrol XL®, Glucotrol®		
	glyburide	Micronase®, Glynase®, Diabeta®		
Thiazolidinedione	troglitazone	Rezulin®		
	rosiglitazone	Avandia®		
	piaglitazone	Actos®		
α-glucosidase inhibitor	acarbose	Precose®		
	meglitinide			
	repaglinide	Prandin®		

After chlorpropamide overdose, urinary alkalinization using sodium bicarbonate can be used to increase excretion.

Lactic acidosis, associated with biguanide therapy, is treated with sodium bicarbonate and hemodialysis, resulting in rapid improvements in acid-base status and removal of metformin from the blood. Persistent lactic acidosis and/or recurrent lactic acidosis is reported and should be monitored for. Along with these options, supportive care is required for all oral hypoglycemics overdoses.

CNYPCC Tidbits answers

1. d
2. a
3. c
4. b

Tox Trivia answers

1. squirrels
2. household iron
3. False, Clostridium botulinum and formed toxin cause toxicity

Patient Follow-up

The patient maintained a blood glucose >90 over 24 hours with no exogenous intravenous glucose required. Initial electrolytes were normal with a serum creatinine of 1.4 mg/dL. Renal lactate measurements revealed an increase of 6 u/L up to 25 u/L, but not outside the therapeutic range and serum bicarbonate remained normal throughout.

Select References:

Quadrani DA et al. Five year retrospective evaluation of sulfonylurea ingestion in children. J Toxicol Clin Toxicol 1996;34:267-270.

Spiller HA et al. Multicenter case series of adult metformin ingestion.(abstract) & Multicenter case series of pediatric metformin ingestion.(abstract) J Toxicol Clin Toxicol 1999;37:639-640.

Boyle PJ, Justice K, Krentz AJ et al. Octreotide reverses hyperinsulinemia and prevents hypoglycemia induced by sulfonylurea overdoses. J Clin Endocrinol Metab 1993;76:752-756.

THE "SPI" CORNER – TOPIC: CARBON MONOXIDE

Contributed By: Nancy O'Neil, R.N., CSPI

Carbon monoxide (CO) forms as a result of the incomplete combustion of carbon containing material. Some examples of sources of exposure include exhaust from malfunctioning furnaces, gas kitchen stoves and automobiles. Furniture stripper, methylene chloride, is converted to CO in vivo.

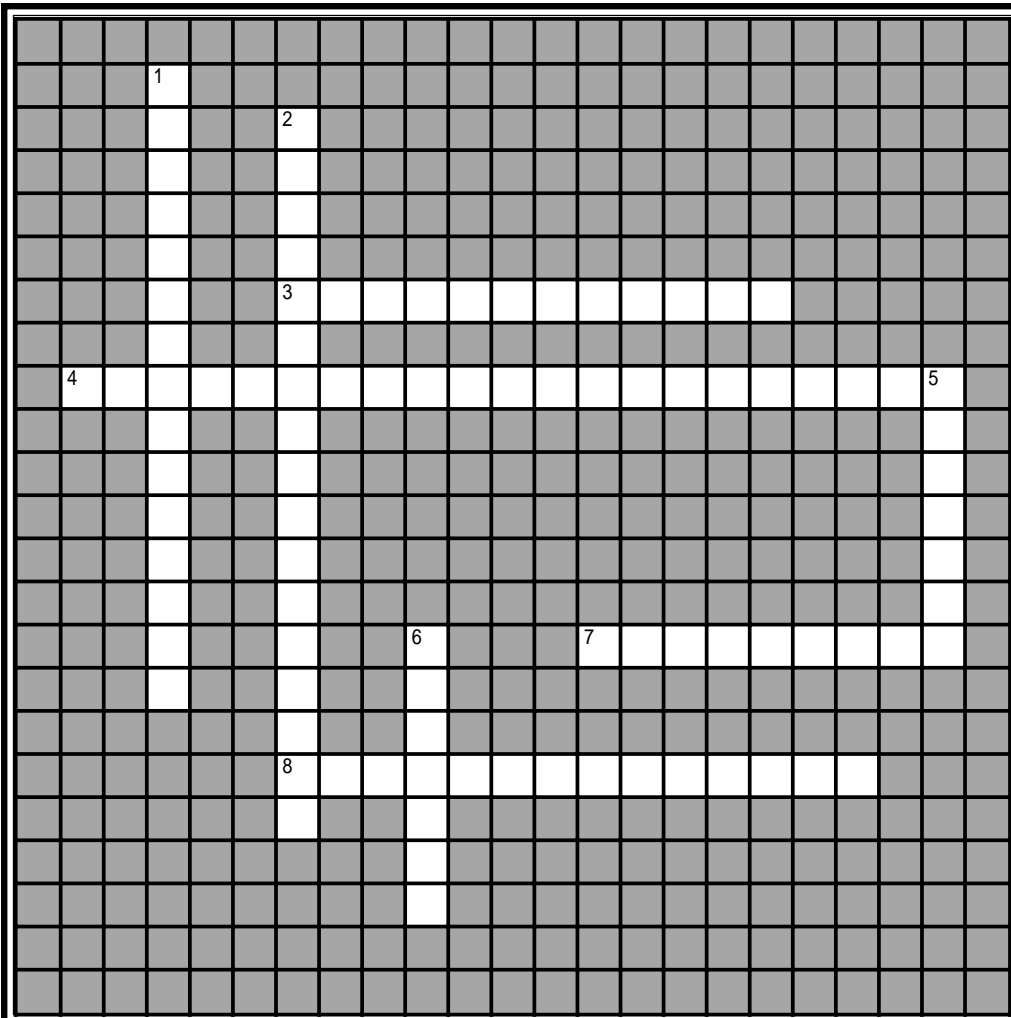
Acute toxicity from CO results in impaired oxygen delivery and utilization, which leads to cellular hypoxia. Initial symptoms may be easily confused with a variety of other medical illnesses. Typical manifestations of acute mild poisoning consist of lethargy, headache, dizziness and nausea. Moderate effects include chest pain, blurred vision, dyspnea on exertion, tachycardia, tachypnea, cognitive defects and ataxia. Severe poisoning results in seizures, coma, dysrhythmias, hypotension, myocardial infarction and death. CO levels are very loosely associated with manifestations of CO poisoning, with any level >10% indicating significant exposure. Persistent delayed effects seen after significant CO poisoning can include dementia, amnesic syndromes, psychosis, parkinsonism, chorea,

cortical blindness, peripheral neuropathy and incontinence.

Patients at particular risk include those with increased respiratory rates such as children, and pregnant patients. Fetal hemoglobin binds more efficiently and longer to CO, placing those patients at excessive risk.

Treatment of CO poisoning includes removal from the environment, oxygen and in some cases hyperbaric oxygen therapy. Oxygen decreases the half-life of CO that is acting on red blood cells. Hyperbaric oxygen further decreases the half-life of hemoglobin bound CO and may, in addition, provide protection from severe delayed manifestations for those at risk. Patients who should be considered for hyperbaric oxygen therapy include moderate-severely poisoned patients and patients with elevated levels >20-25%.

Prevention includes proper installation and maintenance of appliances. In addition, commercially available CO detectors are exquisitely sensitive, even to low levels of CO in the atmosphere, and provide an early warning that a source of CO is in the area.



CAUSES OF SPRING FEVER (HYPERTHERMIA)

Contributed by; Deborah Anguish, RN, CSPI

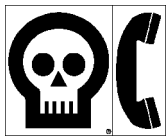
CLUES:
DOWN

1. Blind as a bat, mad as a hatter, dry as a bone
2. Drug interaction, usually involves SSRI's, or MAOI's
5. Over the counter pain and fever reducer
6. Powder of abuse

ACROSS

3. Too much of the older medication, replaced by Synthroid®
4. Rare inhalational anesthetic reaction
7. Microbial or viral
8. Inhalation of burning metals

Across: 3. Thyroid storm, 4. Malignant hyperthermia, 7. Infection, 8. Metal fume fever
Down: 1. Anticholinergic, 2. Serotonin syndrome, 5. Aspirin, 6. Cocaine



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July, 2000

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CNYPC TIDBITS:

Match the drug with the measurement in humans:

1. APAP (acetaminophen)
 - A. 24 hour urine
2. ASA (aspirin/salicylate)
 - B. Sequential timed levels
3. Mercury
 - C. 4 hour after ingestion only

TOX TRIVIA:

Match the Metal with the syndrome:

- | | |
|------------|--------------|
| 1. Lead | A. Plumbism |
| 2. Mercury | B. Itai Itai |
| 3. Cadmium | C. Acrodynia |

Case History

Contributed by: Richard Cantor, M.D., FACEP, FAAP

HEAT ILLNESS

Introduction:

A 75 year old male ingests all of his oral hypoglycemo maintain a consistent body temperature within a narrow range. Elevation of body temperature occurs when:

1. Regulatory mechanisms are overwhelmed at extremes of environmental heat.
2. Endogenous heat production exceeds the physiologic dissipation capacity.
3. Disease processes or drug effects interfere with normal thermoregulation.

Thermoregulation:

The body tries to maintain a careful balance between heat gain and heat loss. Heat gain is based on many factors including the basal metabolic rate and increases nearly tenfold by either drug effects or vigorous exercise. Exogenous gains in heat refer to either exposure to sunlight, high ambient temperatures, or situations of high humidity.

Mechanisms of heat loss are many. Radiation refers to the transfer of heat via electromagnetic waves and is ineffective at body temperatures over 35 degrees centigrade. Convection is defined as the transfer of heat via circulation of air or water vapor. It accounts, in normal settings, for 10 percent of thermal regulation. Convection is the transfer of heat from direct contact to cooler surfaces. This is a minimal contributory factor in heat loss. Evaporation is the process of heat loss via vaporization of water from skin. At baseline it accounts for nearly 20 percent of thermal regulation. This increases dramatically with exercise and sweating.

When heat gain exceeds heat loss, the body responds in an attempt to maintain a consistent temperature. Maximal basal sweating will equal 1 liter per hour. Exercise can increase this up to 3 liters per hour. Sweat glands are traditionally divided into two groups, the apocrine and eccrine. The apocrine glands are predominantly in the axilla and are adrenergically innervated. The eccrine glands are the "thermal sweat glands" and exist throughout the body. They are innervated by cholinergic transmission and have the ability to alter the electrolyte content of sweat. In extreme situations sweat may contain nearly 99.5 percent water.

Cardiovascular effects in response to heat stress include an increase in heart rate and a decrease in systemic vascular resistance. Blood flow is often redistributed, with shifts towards the skin at the expense of the splanchnic circulation. Exercise will also shift blood to exercising muscles. Overall, plasma volume can decrease by as much as 25 %. Other global effects of heat stress include a decrease in renal blood flow, increases in respiratory rate, secondary respiratory alkalosis, and increased production of aldosterone and renin.

Acclimatization refers to the process of decreased heat production for a given unit of work. In general it takes five days for partial and two weeks for full acclimatization to occur. There is also a composition change within the type of sweat produced with decreases in excreted amounts of sodium and chloride.

HEAT ILLNESS (CONT.)

Minor Heat Illness Syndromes

Heat Edema – This is transient and self-limited, is predominant in the hands, feet and ankles and occurs early after exposure to high ambient temperatures.

Heat Tetany – Heat tetany is also self-limited and caused by hyperventilation in response to high temperatures.

Heat Syncope – Vasodilatation, decreased venous return to the heart, decreased cardiac output, and some degree of ischemia occur after high environmental temperatures resulting in orthostatic dizziness or syncope.

Heat Cramps – Heat cramps are most commonly encountered in intensely worked the muscles of acclimatized individuals, especially the calves. They are noted to occur during active cooling of the muscle. The proposed mechanism involves large amounts of sweating with pure water repletion leading to progressive hyponatremia. The cramps are brief (seconds to minutes), intermittent and painful. Measurements of CPK can demonstrate a five fold increase, but full blown rhabdomyolysis is rare. The treatment of heat cramps is rapid salt supplementation.

Major Heat Illness Syndromes

Heat Exhaustion This represents the most common clinical heat illness encountered by most clinicians. In many cases it may be difficult to distinguish from heat stroke and is a diagnosis of exclusion. Usually the core body temperature is less than 39.5 degree centigrade with mild CNS symptoms. Headache, nausea, vomiting, light-headedness, malaise, and myalgias can also occur.

Heat exhaustion is divided into two forms; however, it rarely presents purely as one form. Sweating with adequate water but inadequate salt repletion causes pure salt depletion heat exhaustion. It tends to occur in non-acclimatized people. Complaints include weakness, fatigue, headache, nausea, vomiting, diarrhea, and muscle cramps. Patients will often be tachycardic, hypotensive, and pale but dehydration and hyperthermia are uncommon. Laboratory abnormalities include hyponatremia, hypochloremia, and low urinate FeNa. Sweating with adequate salt but inadequate water repletion causes pure water depletion heat exhaustion. It is seen in predominantly two patient populations. Athletes and new recruits who exercise with limited water repletion constitute the first group. The elderly, very young or debilitated without access to water comprise the second group. Here, progressive dehydration causes elevations of serum sodium along with hyperthermia. Untreated patients may progress to heat stroke. Clinically patients rapidly development of symptoms including thirst, fatigue, weakness, confusion, anxiety, and incoordination.

Heat Stroke

This uncommon form of heat illness constitutes a true medical emergency. Morbidity is determined by the duration of the hyperthermia. Aggressive cooling measures are critical. Exposure to temperatures over 42 degrees centigrade causes uncoupling of oxidative phosphorylation, leading to enzymatic arrest and intravascular fluid collection. Cellular proteins denature with widespread necrosis.

Heat stroke typically involves the precipitous onset of delirium or coma after a history of exposure to elevated ambient temperature or excessive exercise. Medical problems or medication use may predispose individuals to heat stroke.

The physical examination includes a body temperature over 41 degrees centigrade with tachycardia, up to 200 beats/minute. Blood pressure may be normal with a widened pulse pressure. Hallmark CNS findings include coma, delirium, seizures, or behavioral changes. One may also see posturing, aggressive behavior, or cerebellar findings. Focally is rare and if present, suggests another problem. Seizures occur in 25 to 50 percent of patients.

Other Organ System Involvement in Heat Stroke

Hemologically, DIC is seen early in severe heat stroke, particularly after exertion. DIC represents the most common cause of death in heat stroke. Here, endothelial damage leads to the release of tissue factors. Liver damage may also occur hypoglycemia should be monitored for in hepatically injured patients. Rhabdomyolysis and myoglobinuria are common and may result in oliguric renal failure one quarter of patients.

Electrolyte and acid base imbalances are common. Wide fluctuations in serum potassium occur, especially after renal failure. Respiratory alkalosis is present in most patients. Profound metabolic acidosis is the end product of all heat stroke syndromes.

Differential Diagnosis of Heat Stroke

Infections including meningitis, encephalitis, or sepsis should be examined for. Stroke, thyroid storm and pheochromocytoma syndromes are often confused with heat stroke. Also, exposure to drug and toxic agents may mimic and result in similar thermoregulation disorders.

Laboratory testing should include an arterial blood gas, CBC, clotting studies, electrolytes, cardiac enzymes and liver function studies. Urinalysis should include osmolarity and electrolyte measurement. All patients require cerebral CT scanning for evaluation of intracranial processes. Some patients may require infectious assessment.

Treatment of Heat Illness

In general, treat as if heat stroke were present. Rapid correction of hyperthermia results in a better the clinical outcome. "ABCs" should be maintained in heat illness patients with careful attention to the maintenance of normal peripheral circulation.

Cooling Measures

In general the goal is rapid cooling to 39 degrees centigrade. This represents the cornerstone of therapy. Remove the patient from the hot environment. Pre-hospital cooling measures can include the removal of clothes, the provision of a wet sheet and the application of ice to the groin or axilla. Rectal probes represent the most commonly used method of temperature monitoring, although there is a lag behind the core temp.

Immersion Techniques

Rapid temperature reduction will occur with immersion. Rates of up to 2.5 degrees centigrade per minute have been reported. Drawbacks include poor availability, impractical and cumbersome technique and the potential for vasoconstriction. In addition, patients may shiver which will contribute to increases in body temperature. Finally, one third of patients exposed to immersion will demonstrate overcooling. Iced gastric lavage represents an additional useful mechanism to lower body temperature. It is minimally evasive and will often result in cooling rates up to 0.15 degrees centigrade per minute. Another method includes iced peritoneal lavage. This

HEAT ILLNESS (CONT.)

mechanism is invasive, takes a great deal of time to carry out and should be reserved for patients not responding to usual treatment mechanisms. The provision of cooled intravenous fluid is not effective.

Evaporative Cooling

This involves the spraying of tepid water on the patient with the use of fans to evaporate fluid at the skin level. Cooling rates will approximate 0.1 to 0.2 degrees centigrade per minute.

Special situations may occur in the cooling of the hyperthermia patients. If severe shivering occurs, benzodiazepines should be administered which can also be used to treat agitation. Fresh frozen plasma and platelets should be administered in patients with severe DIC.

The prognosis of patients with heat stroke is directly related to the duration and height of body temperature the individual has been exposed to. A Delay for two hours is associated with a 70% mortality rate. Survivors may also suffer neurologic damage. Global poor prognostic factors include body temperature over 42.2 degrees centigrade, SGOT greater than 1,000, DIC, and coma greater than four hours.

Drug Effects On Thermal Regulation

Many drugs and toxins have pharmacological effects that interfere with thermal regulatory responses. These are listed in the Table Abstracted from Goldfrank's Toxicologic Emergencies, 6th Edition:

Effects of Drugs and Toxins That Predispose to Hyperthermia.

1. Impaired cutaneous heat loss
 - a. Vasoconstriction (alpha adrenergic stimulation) Amphetamine, Cocaine, Ephedrine, Phenylpropanolamine, Pseudoephedrine
 - b. Sweat gland dysfunction (anticholinergic effects) Antihistamines, anticholinergics, neuroleptics, Cyclic antidepressants
2. Myocardial depression
Antidysrhythmic agents, Beta adrenergic antagonists, Calcium channel antagonists
3. Uncoupling of oxidative phosphorylation
Pentachlorophenol, Dinitrophenol, Salicylates
4. Increased muscle activity
Caffeine, Isoniazid, Lithium, MAO Inhibitors, PCP, Strychnine, Sympathomimetic agents

Hyperthermia Drug-Related Syndromes

Neuroleptic Malignant Syndrome

Neuroleptic malignant syndrome (NMS) is characterized by hyperthermia, muscle rigidity and other extrapyramidal effects, autonomic dysfunction and altered levels of consciousness. This rare sequela of neuroleptic treatment occurs after use of phenothiazines, butyrophenones, thioxanthenes, and loxapine. Typically there is a history of high initial dose with rapid escalation and usage.

The pathophysiology of NMS includes central dopamine blockade. The diagnosis of NMS is difficult and is often exclusionary. If all of the manifestations of NMS are present and no other obvious causes can be found, one can consider NMS as the primary diagnosis.

Treatment of NMS includes rapid external cooling. The hyperthermia seen in NMS will not respond to antipyretics. There have been anecdotal reports of success with bromocriptine acting as a dopamine agonist. Dantrolene sodium, which inhibits the release of calcium from the sarcoplasmic reticulum, has also been used with varied success. Because NMS is primarily a disease process involving the CNS, there is no derangement of calcium transport in the skeletal muscles as seen in malignant hyperthermia, which responds to dantrolene almost immediately.

Serotonin Syndrome

Serotonin Syndrome is difficult to distinguish from NMS as it also results in symptoms including altered mental status, autonomic instability and altered muscular tone. Here excessive serotonin (5HT_{1a}) receptor stimulation results in an idiosyncratic response. Distinctions from NMS include the drug used and time-frame of the disorder. Serotonin syndrome occurs rapidly (1-2 hours) after exposure to serotonergic drugs or drugs capable of serotonergic effect. Common examples include MAOIs, SSRIs, TCAs, other antidepressants, meperidine, lithium, and dextromethorphan. The syndrome also resolves more quickly, usually within 24 to 48 hours after discontinuation of the offending agent. Treatment is similar including supportive care, cooling and sedation. Some have found success using serotonin antagonists including cyproheptadine, for less severely affected individuals.

Malignant Hyperthermia

Malignant hyperthermia (MH) is a genetic disease with autosomal dominant inheritance involving muscle hypermetabolism associated with an increase in myoplasmic calcium triggered by exposure by certain anesthetic agents. Reported incidences are 1 in 15,000 children and 1 in 50,000 adults.

Identified causative agents include succinylcholine and potent volatile inhalation anesthetics. Manifestations result from hypermetabolism resulting in muscle contractions. Continuous calcium reuptake causes depletion of cellular ATP, excess oxygen consumption, and carbon dioxide production. Hyperkalemia is often seen and may be life-threatening. The most sensitive clinical sign of MH involves an abrupt and unexplained increase in the end tidal CO₂. Hyperthermia is actually a late sign of MH.

Treatment includes removal of the offending drug and dantrolene sodium. Dantrolene inhibits the release of calcium from skeletal muscle sarcoplasmic reticulum, resulting in a disassociation of excitation and contraction coupling.

Select References:

Anderson RJ, Reed G, Knochel J. Heatstroke. *Ann Intern Med* 1983;28:115-140.

Addonizio G, Susman VL, Rother SD. *Neuroleptic malignant syndrome: review and analysis of 115 cases*. *Biol Psychiatry* 1987;22:1004-1020.

Sternbach H. *The serotonin syndrome*. *Am J Psychiatry* 1991;148:705-713.

CNYPCP Tidbits answers

1. C
2. B
3. A

Tox Trivia answers

1. A
2. C
3. B

THE "SPI" CORNER – TOPIC : TOXICOLOGY DRUG LEVELS

Contributed By: Deborah Anguish, RN, CSPI

Although most toxicology treatment decisions are based on clinical findings, drug levels can also be useful in some cases. Many drug levels are easily detectable in the blood or urine. They can be useful in the evaluation of intentional, unintentional, or therapeutic error exposures.

Most common laboratory identified drugs require serial levels for assessment. Serial levels should be obtained and timed every 1 to 2 hours until the peak is seen and less often after. Serial levels are recommended are aspirin, phenobarbital, carbamazepine, digoxin, lithium, theophylline, valproic acid, and phenytoin.

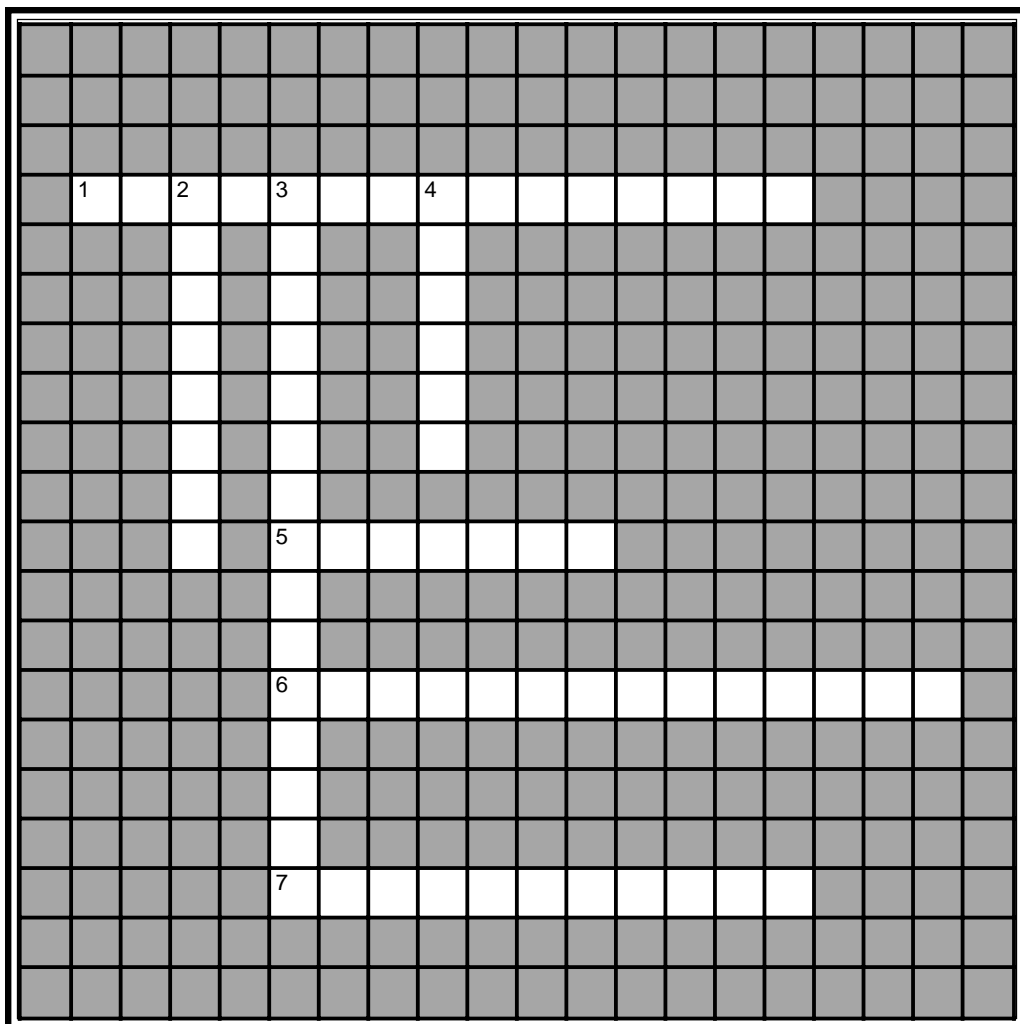
Alternately, some drugs require a single level be drawn at a specific time in order to be useful. These drugs include iron (4 to 6 hours post ingestion), methotrexate (12, 24, and 48 hours after ingestion) and acetaminophen (4-24 hours after ingestion). In fact, acetaminophen levels are performed on all

suspected intentional overdoses, due to 1/500 patients requiring an antidote (determined by level) without a history of ingestion.

Carbon Monoxide and alcohols (ethylene glycol, methanol, and ethanol) require a single level done as soon as possible. If the patient requires treatment (i.e. hemodialysis), a single level should be repeated to determine if further treatment is required.

Spot urine tests for heavy metals are not clinically useful, however, 24-hour urine samples can provide valuable information

Toxicology screens tell whether the person has been exposed to a substance that will react with the screen. It is not quantitative, and in many cases is not sensitive or specific enough to be clinically useful. There are some cases where toxicology screens useful, such as with legal and childcare issues, but only if performed and confirmed correctly.



TOXIDROMES:

Contributed by; Teesh Guentner, RN, CSPI

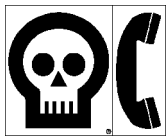
CLUES:
ACROSS

1. hypertension, tachycardia, hyperthermia, diaphoresis, mydriasis
5. lethargy, nausea, vomiting, hyperreflexia, myoclonus, tremor, seizures
6. high anion gap metabolic acidosis, renal toxicity, oliguria, hypocalcemia
7. salivation, lacrimation, urination, defecation, bronchorrhea, emesis, muscle fasciculations, weakness

CLUES:
DOWN

2. high anion gap metabolic acidosis, snow-field vision, abdominal pain
3. hypertension, tachycardia, hyperthermia, dry flushed skin
4. miosis, central nervous system depression, respiratory depression

Across: 1. sympathomimetic, 5. lithium, 6. ethylene glycol, 7. cholinergic
Down: 2. methanol, 3. anticholinergic, 4. opioid



Central
New York
Regional
Poison
Control
Center

The CNYPC

October, 2000

Toxicology Letter

Vol. V No. 4

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SCHEDULED EVENTS:

Emergency Medicine Grand Rounds

NEW LOCATION & DAY:

Health Sciences Library Room 318

Second Wednesday of the Month, 11:00 AM

October 11, 2000,

November 1, 2000 Toxicology Teaching Day

December 13, 2000

Toxicology Case Conference

CNYPC, 550 E Genesee Street

Poison Center Conference Room

Every Thursday 1:30 PM – 2:30 PM

PROGRAM ANNOUNCEMENT:

Please mark your calendars for our Fourth Annual Toxicology Teaching Day on

Wednesday November 1, 2000.

A brochure will be coming shortly.

Please call 464-7078 for more information.

CNYPC TIDBITS:

1. How can silica gel be toxic?
2. What potentially lethal toxin can be found in gun bluing solution?
3. What toxic gas is formed when you pour an acid down a cast room drain?

TOX TRIVIA:

1. Seafood can cause benign elevations in arsenic levels
2. Hydrofluoric acid can readily be found in the home in the form of a wheel cleaner
3. Muscle rubs can contain high concentrations of salicylates or capsaicin cream (hot peppers)

Case History

Contributed by: Deborah A. Anguish RN, CSPI

UPDATE ON RAVES AND CLUB DRUGS?

Case: A 22 year male was brought to emergency care by friends who reported that they were at a "Rave" when their friend collapsed, became incontinent, and had a seizure. A history of experimenting with GHB and Ecstasy was given. While in the ED, the patient required mechanical ventilation due to lack of respiratory effort. He was unresponsive, even to painful stimuli. Initial vital signs included: heart rate; 80/minute, and blood pressure; 120/80 mmHg. Physical examination was not contributory.

What is a "Rave"?

A Rave is a giant dance party where young adults can dance all night. They are typically held in dance clubs or warehouses. Ethanol is not sold at these clubs, as their target audience is teenagers and underage college students. This setting is a haven for sellers of drugs that are touted as being designer drugs, which are newer, better, and with less side effects. While not all raves include drug use, these large gatherings of young middle class dancers will attract drug sellers and despite the fact that ethanol is not sold at these clubs, participants may obtain ethanol-containing beverages in order to mix their drugs. This is referred to as "cocktailing". The most popular drug used at raves across the United States is Ecstasy, but many other drugs can be found such as Ketamine, Nitrous Oxide, GHB, and LSD. To aid in psychedelic experiences, "ravers" often carry glow sticks to wave around and use surgical masks on their face lined with Vicks vapor rub to enhance the sense of smell.

LSD

LSD was developed in 1938, marketed in 1947 and banned in 1966. Used heavily in the 60's and 70's, its use had declined until recently. It is now being used by high school students, and is associated with raves. Its most common alias is acid. LSD ingested from tablets, capsules, and most commonly, liquid impregnated blotter

UPDATE ON RAVES AND CLUB DRUGS?

(CONT.)

paper. Onset is 30 to 60 minutes post ingestion, peak is 3 to 5 hours, and its duration of effects is from 6 to 12 hours. The hallucinogenic effects seen after LSD use is thought to be due to actions on serotonergic neurons. These effects are unpredictable and dependent on dose, mood, personality, expectations, and surroundings.

Sympathomimetic effects often precede hallucinogenic effects.

The desired hallucinogenic effects are altered perceptions, illusions, and hallucinations. Synesthesias are common—confusion of senses i.e. seeing music. Most LSD users don't exhibit severe signs of toxicity and therefore never present to emergency care facilities. Patients that do present are those patients who are either found by their family hallucinating, or who are having an acute psychotic episode from a "bad trip".

Ecstasy

Ecstasy is the slang term used for Methylenedioxymethamphetamine (MDMA). It is also known as XTC, X, Adam, Clarity, and Lover's speed. Other common terms used include "trippin" while using LSD, and "rolling" while using MDMA. MDMA was developed in the early 1900's, as an appetite depressant. MDMA has about one-tenth the CNS stimulant effect of amphetamine. It is considered a hallucinogenic amphetamine, with effects of a hallucinogen, and an amphetamine combined. The hallucinogenic effects are probably due to its ability to cause the release of serotonin, similar to mescaline. Desired effects from this drug are hallucinations, feelings of peacefulness, acceptance, and empathy, and the ability to stay awake to dance all night. According to the DEA, MDMA is commonly manufactured in the Netherlands and Belgium for about one dollar a pill. The drug is transported into the United States by Israeli organized crime factions and then bought by distributors for 6 to 7 dollars a pill. Ultimately, each pill is sold for 20 to 40 dollars a pill to consumers. MDMA is usually ingested as a tablet, has an onset of 20 to 60 min, peaks at 1 to 5 hours, and has a duration of action of 3 to

6 hours. Adverse effects are similar to those expected after overdoses of sympathomimetic drugs and include effects such as hypertension, tachycardia, hyperthermia, seizures and renal failure. Expected minor side effects are teeth grinding (they suck pacifiers and lollipops to help), and dehydration (they carry bottled water or fruit juices to help this). MDMA is considered a neurotoxin. Research has demonstrated a relationship between chronic use of ecstasy and long-term neurologic damage, specifically to neurons that are responsible for the release of serotonin. Manifested symptoms may include sleep disturbances, depression and memory difficulties. Treatment includes aggressive supportive care with careful attention to temperature and excessive muscle activity. Due to diaphoresis and increased physical activity caused by adrenergic over activity and the environment of a hot crowded dance area dehydration is likely and fluids should be administered. Increases in temperature and excess muscle activity should be treated by judicious use of active cooling measures in conjunction with benzodiazepines.

Ketamine

Ketamine is also known as K or Vitamin K or Special K. Ketamine has anesthetic, amnesic and analgesic properties, and is structurally similar to phencyclidine (PCP). Ketamine and PCP block the receptor NMDA, an excitatory amine. A street dose costs approximately \$20.00. Ketamine is a dissociative anesthetic used medically in children and in animals. Ketamine is able to separate perception from sensation, which leads to its abuse. Onset of pharmacologic effects can be anywhere from 4 to 20 minutes depending on the route of administration. Ketamine can be snorted, ingested, or be laced on marijuana. The effects last from last from 30 min to 2 hours. The desirable effects after use are those associated with emergence delirium. Reported effects include feelings of weightlessness, body dissociation and near death experiences. This is a near death experience that is sometimes described by users as coming out of a "k-hole".

UPDATE ON RAVES AND CLUB DRUGS?

(CONT.)

The sensation of loss of motor control can correlate with real muscle loss of control and dystonia and nystagmus. Panic attacks, and aggressive behavior is also seen in some cases. When mixed with other drugs such as GHB or alcohol there is increased potential for central nervous system and respiratory depression. Rarely, seizures, increased intracranial pressure and cardiac arrest occur. Treatment for Ketamine overdose includes aggressive supportive care using benzodiazepines for sedation.

Nitrous Oxide

Nitrous Oxide gas commonly used as an anesthetic in dentistry is commonly referred to as laughing gas. It is also used in the dairy industry as a mixing and foaming agent. It is commonly known to abusers by the name "whippets". Finally, it is used in auto racing as a fuel enhancer to boost speed. Nitrous oxide balloons may be sold at rave parties for inhalation. Participant may repeatedly inhale the gas in the balloon until the point of asphyxiation. Desired effects include a sensation of tingling. In medical practice, nitrous oxide is mixed with 25 to 30 % oxygen in order to prevent the asphyxiation effects seen after a relative lack of oxygen. Nitrous Oxide used in this setting will provide sedation starting at inhaled doses of 25% nitrous oxide. Abuse of nitrous oxide typically includes inhalation of 100% nitrous oxide. Death typically occurs as a result of anoxic brain injury. Treatment includes aggressive symptomatic and supportive care. Reports of leukopenia, thrombocytopenia, myeloneuropathy and megaloblastic anemia occur after chronic inhalation of nitrous oxide.

GHB

Gamma-hydroxybutyrate (GHB) is a CNS depressant/anesthetic that can be snorted, taken orally, or inhaled. It is found in both liquid and powder form. GHB is odorless and

colorless, and its use has been reported in cases of date rape. GHB is also called "liquid ecstasy, liquid x, Scoop, Goop, or Georgia Home Boy". It was originally synthesized as a GABA analog that would more easily cross the blood brain barrier. As GHB became less available medically, it was sought out in health food stores. It was sold in health food stores as a bodybuilding supplement reported to increase release growth hormone. This has not been substantiated. Now it is unavailable commercially in the US, however it can be easily manufactured and is also sold in the precursor form, Gamma Butyrolactone (GBL). GHB was initially used as general anesthetic and is used in other countries for these effects as well as for treatment for narcolepsy. GHB interacts with GHB receptors, is a GABA_B agonists and alters dopaminergic activity. Desired effects after abuse include relaxation, euphoria, and central nervous system depression. These effects are greatly enhanced by co-ingestions of other central nervous system depressants including ethanol. Onset is rapid and effects can last up to four hours. After overdose decreased mental status, respiratory depression, and seizures are reported. Treatment for patients who use GHB includes aggressive supportive care. Withdrawal Signs and symptoms are being reported from chronic GHB use. The reported effects are severe agitation, elevated B/P, and Tachycardia within hours of stopping use.

End of Case

After 2 hours, the patient became awake and alert and admitted to ingesting GHB.

Select References:

Craig K. Gomez HF, McManus JL. Bania TC, Severe gamma-hydroxybutyrate withdrawal: a case report and literature review. *Journal of Emergency Medicine*. 18(1):65-70, 2000 Jan.

McCann UD, Merti M, Eligulashvili V, Ricaurte GA. Cognitive performance in (+/-) 3, 4-methylenedioxymethamphetamine (MDMA, "ecstasy") users: a controlled study. *Psychopharmacology* 143(4):417-25 1999 APR. National Institute for a Drug Free America @ www.nida.nih.gov

CNYPC Tidbits answers

1. By causing an obstruction
2. Selenium
3. Hydrogen Sulfide

SPI CORNER TOPIC: GLOW STICKS

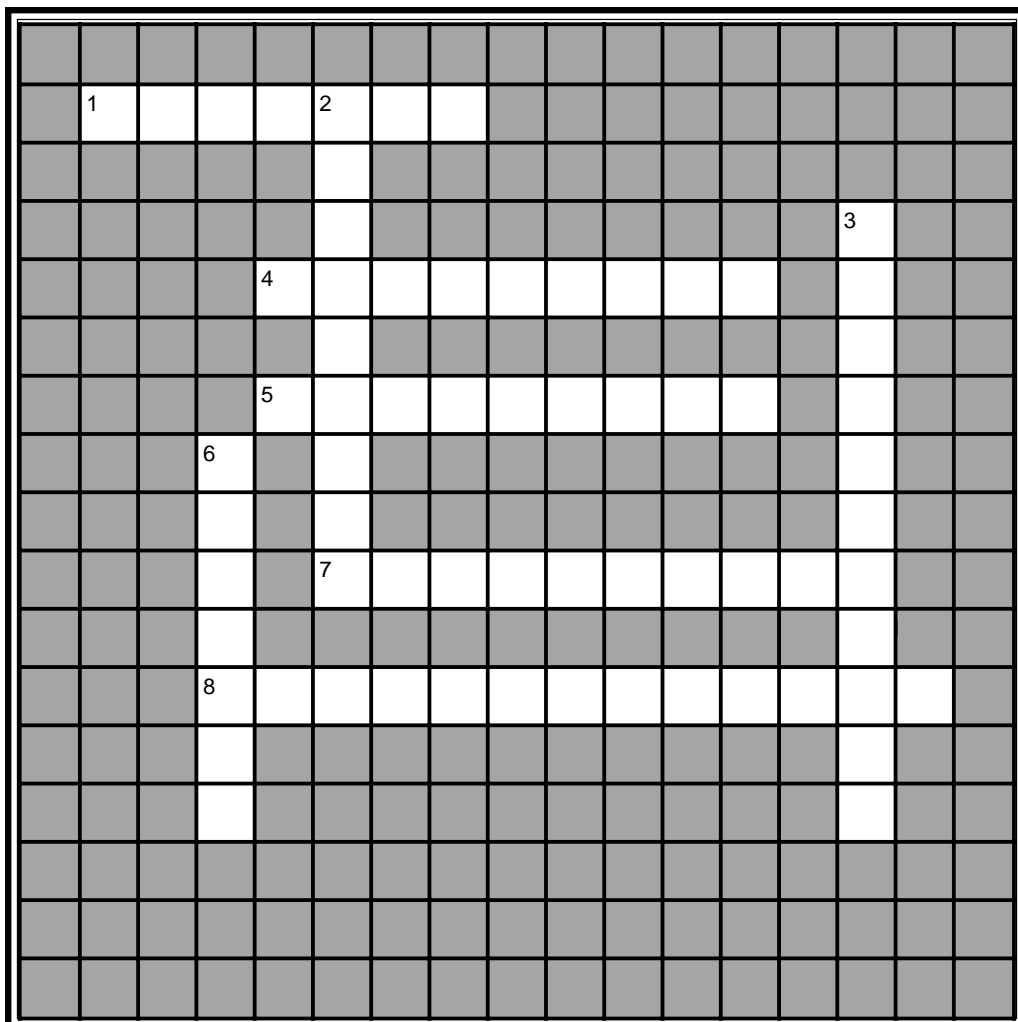
Contributed by: Linda Jutton, R.N., CSPI

During July 4th and Halloween, the Poison Control Center gets many calls regarding exposures to glow sticks or necklaces. A glow stick is a polyethylene tube containing the luminescent component, dibutyl phthalate. This tube also contains another tube that contains the activator component, dimethyl phthalate. When this tube is broken the activator mixes with the luminescent component and a chemical reaction occurs causing the glowing effect. Dibutyl phthalate is also used as a solvent for perfume oil, safety glass, printing inks, paper coatings, and adhesives. It has been used in nail polish, insect repellents, and solid rocket propellants.

Dibutyl phthalate is thought to have low acute toxicity based on animal studies, but contact with any body part may produce immediate stinging

and burning sensations. The PCC has seen oral irritation and occasionally seen blisters to the lips after a child has bitten a glow stick. Some parents have reported that the child's mouth has glowed in the dark. A splash to the eye can produce burning and irritation as well as profuse lacrimation.

Treatment is primarily symptomatic and supportive. Washing of the mouth or ocular flushing using water for 15 minutes is recommended immediately after exposure. Ice chips and popsicles can be used for any continued oral burning sensation. If symptoms are prolonged, an evaluation of the exposed area should occur to check for burns. Most exposures do not result in significant injury.



DRUG STREET NAMES

Contributed by; Teesh Guentner, RN, CSPI

CLUES:
ACROSS

1. Coke, snow, rock, toot, white lady
4. School boy
5. Pot, grass, weed, Columbia herb
7. Speed, upper, bennies,
8. Angel dust, killer hog

CLUES:
DOWN

2. Laughing gas, whippets, poppers
3. Barbs, downers, yellow jacket, red devils, blue devils
6. Booze, hooch

Across: 2. cocaine, 4. narcotics, 5. marijuana, 7. stimulants, 8. hallucinogens; Down: 2. inhalants, 3. depressants, 6. alcohol