New York State Poison Centers
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The NY State Poison Centers

Toxicology *Letter*

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TOXICOLOGY ADVICE CENTERS:

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PROGRAM ANNOUNCEMENTS:

WNY:
FL: Conference, Thursdays • 1:00-2:00pm
CNY: Case Conference, Thursdays • 1:30-2:30pm
NYC: Consultants Case Conference • 1/2/03, 2/6/03, 3/6/03
An Intensive Review Course in Clinical Toxicology • 3/13-14/03
LI: Biological Terrorist Agents • 1/29/03
How to Evaluate and Provide Management to a Posioned Patient • 2/26/03
Cardiac Drug Emergencies • 3/26/03

Please call administrative telephone numbers for more information.

NYPC TIDBITS:

Matching: Match the antidote with the poisoning

A. Atropine
B. Sodium nitrite
C. Flumazenil
D. Naloxone
E. Pyridoxine
F. Sodium Bicarbonate

1. Organophosphate poisoning
2. Cyanide toxicity
3. Benzodiazepine overdose
4. Opioid intoxication
5. Seizure on Isoniazid
6. Tricyclic antidepressant overdose

TOX TRIVIA: PLANTS

1. Cocaine is derived from the leaves of what plants?

2. Marijuana is a common name from the material obtained from this plant.

3. Ephedrine is the active substance in this Chinese plant.

Case History

ACUTE SALICYLATE TOXICITY

Contributed by: Kerry Cronin MD, Thomas Caraccio Pharm D, and Michael McGuigan MD, Long Island Regional Poison and Drug Information Cetner

Case:

A 16 year old male stole a vehicle and lead police on a high speed chase which ended in a collision. The patient told the police that he ingested 500 aspirin tablets six hours previously. He was evaluated at a local emergency department and no significant traumatic injuries were noted. After discharge into police custody, he developed abdominal pain and a rapid respiratory rate and was brought back to the emergency department. Initial laboratory data revealed an anion gap metabolic acidosis. An arterial blood gas analysis noted a pH of 7.44 with a mixed respiratory alkalosis and metabolic acidosis. His initial salicylate concentration, drawn approximately 6.5 hours post-ingestion, was 49 mg/dL.

The patient was given a single oral dose of activated charcoal and was started on intravenous fluid containing sodium bicarbonate and potassium. The poison information center was contacted and recommended the immediate transfer of the patient to a facility with the capability to perform hemodialysis. Repeat salicylate concentrations were done at 10.5h, 16.5h, and 18.5h post ingestion and were 56 mg/dL, 105 mg/dL, and 133.8 mg/dL, respectively. Approximately 20 hours post-ingestion, the patient arrived at a tertiary care center, had a seizure, developed cardiopulmonary arrest, and died before hemodialysis could be initiated. The antemortem salicylate concentration was 503 mg/dL.

What are salicylates and how do they work?

Salicylates are nonsteroidal anti-inflammatory agents commonly used for their analgesic and antipyretic properties. They act on the cyclooxygenase enzymes to impair peripheral and central prostaglandin biosynthesis; they also inhibit platelet aggregation. The usual recommended dose for adults is 325-650mg/dose every 4 hours, and for children is 10-15mg/kg/dose every 4-6 hours with a maximum of 80mg/kg/24h. The toxic dose of salicylic acid is >150mg/kg.[1]

How common is salicylate overdose?

In 2001, there were 20,623 salicylate exposures reported to US Poison Centers, of which 3,232 developed moderate and major outcomes and 72 resulted in death.[2]

What are the toxic effects of salicylic acid, their mechanisms, and the classic phases of acute salicylate intoxication?

Salicylate has a direct stimulatory effect on the respiratory center in the brainstem inducing hyperventilation.[3] Salicylate indirectly affects respiration secondary to skeletal muscle stimulation, resulting in an increase in oxygen consumption and carbon dioxide production.[4] Together these stimulatory effects produce a respiratory alkalosis.[3,4]

Salicylate toxicity classically gives rise to an increased anion gap metabolic acidosis, which is the result of various mechanisms. In

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Table 1

Category of Toxicity	Amount Ingested	Toxic Manifestations
Mild	150-200mg/kg	Nausea, Vomiting, Tinnitus, Hyperventilation and Respiratory Alkalosis
Moderate	200-300mg/kg	Hyperpnea, Fever, Acidosis, Lethargy, Dehydration, Mixed respiratory alkalosis and anion gap metabolic acidosis, Electrolyte disturbances
Severe	300-500mg/kg	Altered level of consciousness, Coma, Convulsions, Pulmonary Edema, Hypotension, Renal Failure, Mixed respiratory alkalosis and anion gap metabolic acidosis, Electrolyte disturbances
Very Severe	>500mg/kg	Potentially Fatal

response to the respiratory alkalosis described above, the kidneys increase bicarbonate and potassium excretion.[5] Impaired renal function secondary to salicylate toxicity leads to the accumulation of sulfuric and phosphoric acids.[6] Salicylates alter carbohydrate metabolism, producing hypoglycemia, and interfere with the Krebs cycle's dehydrogenase and aminotransferase enzymes, resulting in the formation of increased lactate, pyruvate, and ketones.[7] In addition, salicylates interfere with cellular metabolism by uncoupling mitochondrial oxidative phosphorylation, resulting in decreased production of ATP and increased acid production and heat generation leading to hyperthermia.[8] Finally, salicylates themselves are weak acids.[7] ***Together these effects of salicylates pr***Salicylates decrease the production of prostaglandins. This may result in gastritis, nausea and vomiting because prostaglandins normally provide gastric mucosal protection.[9] Antiplatelet activity is a well-known effect of acetylated salicylate (aspirin) and rarely hemorrhage may occur with toxicity.[5] Chronic administration of salicylates in large doses causes damage to the liver resulting in prolonged prothrombin time, decreased factor VIII production, and increased capillary fragility, although permanent damage to the liver is rare.[9] Electrolyte disturbances include hypocalcemia, hypomagnesemia, hypokalemia, and hypoglycemia.

The pathophysiologic changes attributable to salicylate toxicity result in various clinical manifestations depending on the amount ingested (Table 1).[5,9,10,11,12]

The most important sign of severe intoxication is an altered level of consciousness. Rare complications of salicylate overdose are GI perforation, inappropriate secretion of antidiuretic hormone, pancreatitis and cerebral edema.

What is the proper treatment of salicylate overdose?

Decontamination serves to reduce the absorption of salicylate in overdose situations and numerous decontamination methods are debated in the literature. Acetylsalicylic acid (ASA) absorption is reduced with activated charcoal administration.[13] The recommended dose of activated charcoal is 1-2g/kg, recommended if the patient has ingested a potentially toxic amount of salicylate up to 1 hour previously.[14] There are insufficient data to support or exclude its use after 1 hour of ingestion.[14] Multiple dose activated charcoal (MDAC) is no longer advised in salicylate overdose.[15] Enteric-coated and sustained-release aspirin preparations merit special considerations in regard to GI decontamination.[5] These preparations may be too large for removal by a #40 french gastric lavage tube, may be radioopague depending upon the manufacturer and therefore visualized with abdominal radiographs, and these preparations may form large concretions in the GI tract leading to delayed toxicity.[5] Whole bowel irrigation (WBI) may be considered for potentially toxic ingestions of sustained-release or enteric-coated aspirin tablets[16]. Kirshenbaum et. al. showed that WBI was more effective in reducing the absorption of sustained release aspirin than activated charcoal with sorbitol.[17] Gastric lavage is a consideration, if a life threatening amount was taken, the airway is protected, and the procedure can be undertaken within 60 minutes of ingestion. Although syrup of ipecac is not routinely recommended[19], some toxicologists may advise it in very large ingestions. Despite the above recommendations for GI decontamination, there is extensive variability in the advice given to health care providers offered by poison control centers.[20]

The treatment of symptomatic patients with salicylate ingestion should be started immediately. The Done nomogram, which was created to identify the level of salicylate intoxication that should prompt intervention, is often misused and misunderstood.[5] It is generally considered to be obsolete[5.] The patient's clinical condition and early course should serve as the guide for clinical therapy[5] After initial stabilization, careful history and physical examination, an assessment of the patient's fluid balance and electrolyte status is necessary. ECG, pulse oximetry, cardiac monitoring, serum electrolyte levels including magnesium and phosphorus, glucose, ABG, renal and hepatic functions, prothrombin time, urinalysis, abdominal radiography, acetaminophen and salicylate levels are recommended. The ABG, electrolytes, glucose level and salicylate level should be repeated in moderate and severe overdose every two hours until the levels are declining and the patient's clinical condition stabilizes.

The goal of salicylate management is to minimize the CNS salicylate concentration and to facilitate salicylate excretion.[5] Intravenous sodium bicarbonate, through alkalinization of the blood and urine, keeps salicylate out of the CSF and enhances urinary salicylate excretion.[21] NaHCO3 should be administered in all but mild salicylate overdoses to produce a pH of 7.4-7.5 and urine pH>7.[22] Adults should receive a bolus 1-2 mEq/kg of sodium bicarbonate followed by an infusion of 100-150mEq NaHCO3 added to 500-100ml of 5% dextrose; children should receive a bolus of 1-2mEq/kg of NaHCO3 followed by an infusion of 1-2 mEq/kg added to 20 mL/kg of 5% dextrose.[22] Target urinary output is >2ml/kg/hr.[22]

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Intravenous fluids should contain glucose and potassium. Along with aggressive fluid and electrolyte replacement and alkalinization of blood and urine, symptomatic and supportive care should be instituted. Seizures should be treated with diazepam or lorazepam. Pulmonary edema management consists of fluid restriction, high FiO2, mechanical ventilation and PEEP. Hyperpyrexia is managed with external cooling measures.

Extracorporeal measures are indicated in severe salicylate intoxication. [21] Hemodialysis is considered the best choice because it can rapidly correct acid-base and electrolyte abnormalities while removing salicylate from the blood.[5] Indications for hemodialysis include renal failure, congestive heart failure, persistant CNS disturbances, progressive deterioration of vital signs, severe acid-base or electrolyte imbalance despite appropriate treatment, hepatic compromise with coagulopathy, and salicylate level (acute) >100mg/dL.[21] Higgins et. al. described an interesting case of a man who took two aspirin overdoses in a short space of time, achieving similar blood levels of salicylate and sustaining grand mal seizures on both occasions. On one occasion he was treated with alkalinization and on the other he was treated with hemodialysis; both methods were equally effective in eliminating salicylate over a 24h period, though alkalinization achieved a more rapid initial reduction in blood levels of salicylate.[23]

What is the difference between acute and chronic salicylate overdose?

The presentation of chronic salicylate intoxication is more subtle and difficult to diagnose. [24] Chronic salicylism is more common than generally appreciated and is more serious than acute intoxication because it is often under diagnosed. [24] The mortality rate is high with chronic toxicity and the salicylate plasma concentration does not often correlate with the clinical manifestations of toxicity. The young and elderly are often victims of therapeutic errors and are at risk for chronic salicylism. Chronic salicylism is associated with exaggerated CNS findings of lethargy, confusion, drowsiness, slurred speech, hallucinations, tremor, agitation, and delerium.[24] Although there is considerable overlap with some of the presenting signs and symptoms of acute salicylate poisoning, there is a slower onset and a less-severe appearance of these signs with chronic toxicity. [21] The cardinal clinical and laboratory features of chronic salicylate poisoning include abdominal pain, tachypnea, encephalopathy, acid-base disturbances, coagulapathy, and adult respiratory distress syndrome. [25]

Case discussion:

Aspirin bezoars, or large concretions, may form after large ingestions of aspirin leading to prolonged absorption. Peak serum salicylate levels may be delayed from 10-60 hours with enteric-coated, sustained-release, or very large ingestions. Although the serum salicylate levels were steadily rising in this patient, appropriate treatment was delayed. Failure of aggressive management in this particular case may have lead to the demise of the patient. Furthermore, despite a history of the ingesting 500 aspirin tablets six hours prior to his presentation, he was discharged without a serum salicylate concentration determination.

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CNYPCC Tidbits answers:

A. 1
B. 2
C. 3
D. 4
E. 5
F. 6

Tox Trivia answers:

1. Erythroxylon coca and Truxillo coca.
2. Cannabis sativa
3. Ma-huang

SPI CORNER TOPIC: IS GASTROINTESTINAL DECONTAMINATION ALL WASHED UP?

Submitted by: The Long Island Regional Poison and Drug Information Center SPI Staff

An important and debated issue in clinical toxicology is whether, when and how to remove ingested poisons from the gastrointestinal tract. Guidelines have been published recently on the use of ipecac syrup, gastric lavage, actiavted charcoal, cathartics, and whole bowel irrigation. The key points regarding these procedures are presented. GI Decontamination (GID) should not be a routine procedure, and should not pre-empt the provision of symptomatic and supportive care. The substance ingested, clinical presentation, and the time of ingestion need to be taken into consideration. GID procedures do not completely evacuate the stomach, and may leave substantial amounts of the ingested substance.

Syrup of Ipecac (SOI)is available as a nonprescription drug to produce emesis and remove ingested poisons from the stomach. However, the amount of substance removed by ipecac is highly variable and diminishes with time. SOI should rarely be used in the Emergency Department. Ipecac may delay the administration of activated charcoal or whole bowel irrigation. Ipecac should not be administered to a patient who has a decreased level or impending loss of consciousness or who has ingested a corrosive substance or hydrocarbon with high aspiration potential.

Gastric Lavage (GL) involves the passage of an orogastric tube and the sequential administration and aspiration of small volumes of liquid to remove toxic substances in the stomach. There is a difference between GL and gastric aspiration (which involves the use of a smaller tube to suck out liquid from the stomach). The amount of substance removed by GL is highly variable and diminishes with time. There is no evidence that its use improves clinical outcome and it may cause significant morbidity. GL should not be considered unless a patient has ingested a potentially life-threatening amount of a poison, the procedure can be undertaken within 60 minutes of ingestionand the airway is protected with the _____.

Activated Charcoal (AC) therapy involves the oral administration or instillation by a tube of an aqueous suspension of AC after the ingestion of a poison. AC physically binds poisons in the gastrointestinal tract, decreasing the extent of absorption of the poison and reducing or preventing systemic toxicity. The greatest benefit from AC is within 1 hr of ingestion. It is contraindicated if airway protective reflexes are lost in a patient who is not intubated; pulmonary aspiration of AC is hazardous.

Cathartics such as accharide cathartics (sorbitol) and saline cathartics (magnesium citrate or sulfate, sodium sulfate) attempt to decrease the absorption of substances by reducing GI transit time. Sorbitol improves the palatability of AC by imparting a sweet taste and by masking the grittiness of the charcoal. A cathartic, with or without AC, does not reduce the absorption of drugs or improve the outcome of poisoned patients. The routine use of a cathartic in combination with AC is not recommended.

Whole Bowel Irrigation (WBI) cleanses the bowel by the enteral administration of large amounts of an osmotically balanced polyethylene glycol electrolyte solution which physically expels intraluminal contents. There is some evidence that WBI decreases the absorption of ingested drugs, but there is no conclusive evidence that WBI improves the outcome of the poisoned patient. WBI may be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs or substances that are not bound by AC (e.g., iron, lithium). WBI is contraindicated in patients with bowel obstruction, perforation, ileus, and in patients with hemodynamic instability or compromised unprotected airways. Administration of AC during WBI is not recommended.

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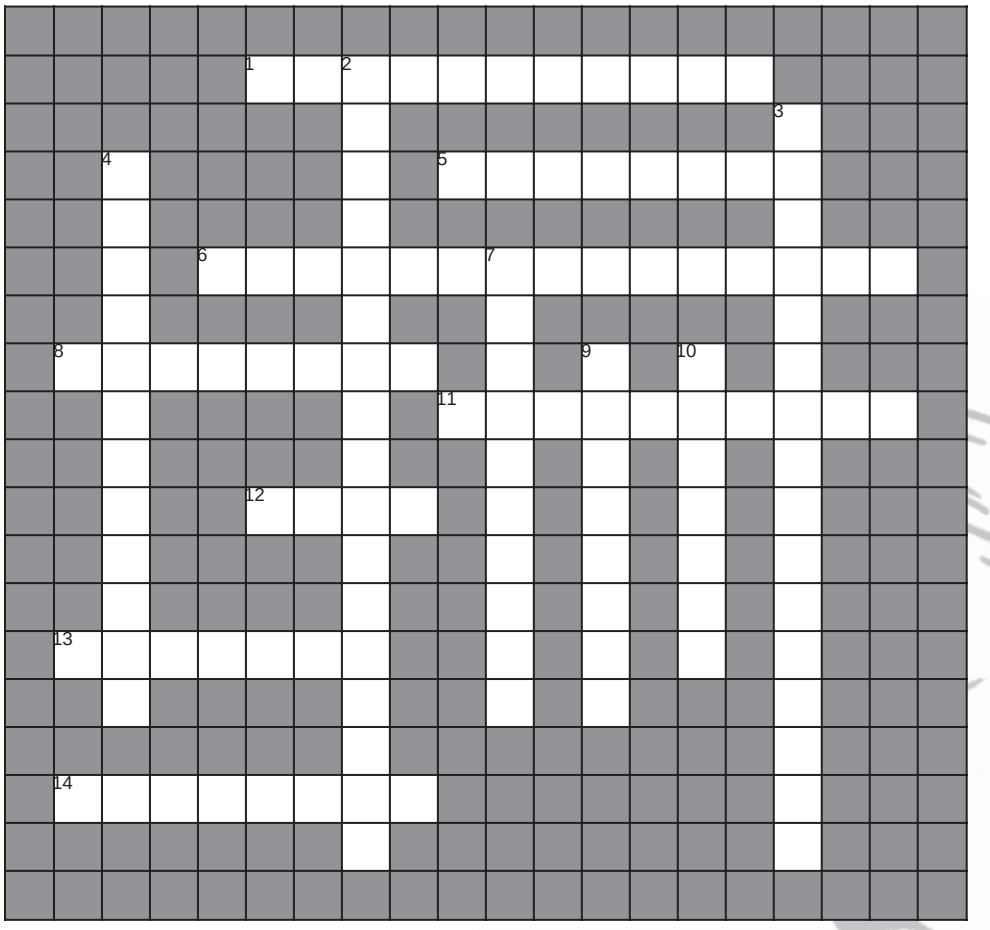
CROSSWORD PUZZLE : COLD SEASON



1. Antidote for acetaminophen overdose
2. Treat this overdose with deferoxamine
3. Pathognomonic rhythm disturbance is bi-directional ventricular tachycardia
4. Overdose causes agitation, tachycardia, mydriasis, urinary retention, and ileus
5. Treatment of ethylene glycol poisoning
6. Alcohol poisoning causing visual disturbances and fundoscopic abnormalities
7. Toxicity causes coarse tremor, rash, diabetes insipidus, fasciculations and seizures
8. First line agent to treat beta blocker overdose
9. Treatment for a patient with lead poisoning and encephalopathy
10. Calcium gluconate gel is used to treat burns caused by this acid
11. Pulse -ox of 85% with chocolate-brown discoloration
12. Spider bite causing necrosis
13. A date rape drug
14. Mushroom toxin

Crossword answers:

1. Nacetylcysteine 2. Iron 3. Digoxin 4. Anticholinergics 5. Fomepizole 6. Methanol 7. Lithium 8. Glucagon 9. Dimercaprol 10. Hydrofluoric 11. Methemoglobinemia 12. Loxoscelesl 13. Rohypnol 14. Amatoxin