

The CNYPCC

Toxicology Letter

Vol. IV 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 15, 1999 February 19, 1999 March 19, 1999

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

PROGRAM ANNOUNCEMENT:

Thank you to all who participated in our 2nd annual Toxicology Teaching Day. If you would like a syllabus, please call us at 315-464-7078. Our 3rd date will be Nov. 5th.

CNYPCC TIDBITS:

- Drug interactions can occur if this common ingredient in cold preparations is taken in conjunction with a MAOI or a SSRI... Dextromethorphan.
- New antidote for ethylene glycol poisoning . . . fomepizole (Antizol ®).
- Marker ingredient causing methemoglobinemia . . . aniline.

TOX TRIVIA:

Matching: Toxin with laboratory finding

- 1. Bromides (Bromoseltzer®)
- 2. Aspirin
- 3. Toluene (airplane glue)
- 4. Iron
- Anion gap metabolic acidosis with appropriate respiratory compensation
- Anion gap metabolic acidosis with too much respiratory compensation
- Negative anion gap metabolic acidosis
- d. Renal tubular acidosis

Case History

Contributed by: Susan Bruce, PharmD Candidate, Christine M. Stork, Pharm.D., ABAT

DRUG INTERACTIONS AND THE CYTOCHROME P450 ISOENZYME SYSTEM

Case 1

A 20 year old presents to the Emergency Department (ED) with a 4 day history of headache, nausea, and vomiting. 3 days prior, she was prescribed ciprofloxacin for treatment of a urinary tract infection. She mentions that she routinely takes ciprofloxacin with her vitamin supplements, and the evening dose with an antacid for calcium supplementation.

Case 2

A 64 year old presents to the ED with palpitations. She experienced 2 syncopal episodes this morning precipitating her visit. She has no prior cardiac history and current medications include cisapride and Prempro. Three days ago, she was given erythromycin for pharyngitis. Initial ECG shows a long QT interval and prominent U waves.

What types of drug interactions are currently known?

Drug interactions can be pharmacokinetic and pharmacodynamic. Pharmacokinetic interactions affect absorption, distribution, metabolism, or elimination. Pharmacodynamic interactions are specific for receptor sites and involve the interplay of or between agonists and antagonists. Categories of pharmacodynamic interactions are antagonistic, synergistic or additive therapeutic effect, synergistic or additive side effect, and indirect pharmacodynamic.

What is the most common identifiable drug interaction?

Drug interactions result in complex interplay causing subtle or overt clinical changes. Pharmacokinetic interactions are the most easy to identify through changes in drug concentrations which can be measured.

Absorption can be altered as a result of amount or rate at which absorption occurs. In case 1, divalent cations (calcium, zinc, magnesium) are binding to ciprofloxacin in the gut to prevent absorption.

The location of drug molecules in the body (distribution) can be altered by several factors. High blood protein bound drugs can be

displaced from proteins by other drugs or disease states and result in increased activity. For example, if a drug is 99% protein bound, a change in binding to 98%, increases the free fraction by 100%. Some drugs that are highly blood protein bound include phenytoin, warfarin, lidocaine and propranolol.

Metabolism can be increased or decreased by various factors including age, genetic makeup, nutritional status, and endogenous chemicals including drugs. In the second case, erythromycin resulted in an increased cisapride concentration. Most metabolism interactions involve the cytochrome P450 isoenzyme system, although others occur.

Elimination drug interactions most commonly involve the kidneys. Drugs and disease states that increase or decrease glomerular filtration or tubular secretion affect drug removal. In addition, altered urinary pH can change the elimination pattern for weak acids and bases that rely on renal excretion.

What is the cytochrome P450 isoenzyme system?

The purpose of drug metabolism is to increase water solubility and facilitate renal excretion. The majority of drug metabolism leads to metabolites with decreased or no activity, but rarely drugs are activated through metabolism (prodrugs). The pathway that is responsible for the majority of drug metabolism is the cytochrome P450 isoenzyme system (CYP). These enzymes can be found in various organs including the intestines, lungs and kidneys, but are predominantly found in the centrolobular location of the liver. Specifically, these groups of heme-containing enzymes that absorb light at a wavelength of 450 nm are found in the lipid bilayer of the endoplasmic reticulum. Collectively, cyto- (hollow vesical), chrome (color), pigment (P) and wavelength (450), constitute the nomenclature cytochrome P450.

Classification of the CYP system involves three levels; family, subfamily, and individual isoenzyme. At least twelve families are identified. More than 30 isoenzymes of the families CYP1, CYP2, and CYP3 have been identified, but those extensively involved in drug metabolism are CYP1A2, CYP2D6, CYP3A4, and CYP2C.

What types of drug interactions can occur via CYP 450 isoenzymes?

CYP interactions are pharmacokinetic and rely upon enzyme inhibition or induction. Enzyme inhibitors prevent metabolism, resulting in higher serum concentrations. Enzyme inducers cause an increase in the synthesis of enzymes, resulting in increased metabolism. Inhibition interactions can be competitive or noncompetitive. Induction reactions occur when blood flow to the liver is increased, or when production of CYP 450 enzymes is increased.

The complexity of these interactions is magnified when considering that drugs can be inhibitors or inducers of more than one CYP isoenzyme. Xenobiotics (drugs and foreign chemicals) can be metabolized by more than one enzyme, making the prediction of drug interactions difficult. **Table 1** is a listing of substrates, inhibitors and inducers for the major isoenzymes involved in significant and potentially life-threatening drug interactions.

What are the non-drug influences of CYP 450?

Other factors not related to drugs that affect metabolism include genetics, comorbidity, age, and tobacco and alcohol history. CYP composition is genetically determined and at least two of the specific isoenzymes are shown to have genetic polymorphism.

As age increases, gastric and intestinal motility, liver mass, hepatic enzyme activity, and hepatic blood flow decrease. Concomitant disease states that decrease renal function, hepatic dysfunction or liver blood flow can lead to decreased metabolism.

Tobacco and alcohol use influences CYP 450. An example is theophylline, which is metabolized by CYP 1A2. Higher doses of theophylline are required to achieve a therapeutic level in smokers due to enzyme induction. Occasional ethanol use inhibits 2E1 activity, is, however, long term ethanol ingestion induces 2E1 enzymes.

The major isoenzymes are CYP; 1A2, 2D6, 3A4, and 2C subfamily. Each isoenzyme has unique characteristics: a. The CYP 1A2 isoenzyme is influenced by environmental factors in addition to drugs; b. The CYP 2D6 isoenzyme is a pathway of many psychiatric and cardiovascular drugs and has extensive genetic polymorphism. 5-10% of Caucasians and 1-3% of Asians and African Americans are poor metabolizers of this enzyme; c. CYP 3A4 is involved in general metabolism; d. The CYP2C subfamily, 2C19 has genetic polymorphism, almost opposite to that of 2D6, in which 3-5% of Caucasians and 20% of Asians and African Americans are reported as poor metabolizers.

What time course is associated with inhibition and induction reactions?

Inhibition occurs rapidly and is based upon drug concentration. Significance varies with drug concentration as well as the half-life of the interacting

DRUG INTERACTIONS AND THE CYTOCHROME P450 ISOENZYME SYSTEM

(CONT.)

drug. The time for maximum drug interaction is the time required to reach a new steady state of the inhibited drug.

The time course of induction interactions depends on the half-life of the inducing agent. The turnover of CYP450 enzymes ranges from 1-6 days. Induction effects are seen within the first two days, but may take more than one week for maximal effect.

How do I tell which interactions are significant, and what are the options for management?

Medications that have narrow therapeutic indices should be closely monitored (ie. warfarin, theophylline, antiarrhythmics, anticonvulsants, antineoplastics, immunosuppressive agents), as small changes in their metabolism can have profound effects.

Patients presenting to emergency care as the result of a drug interaction should be managed according to the demonstrated toxicity. Depending on the change in serum concentration of the affected drug, the dose could be adjusted to increase or decrease the concentration to achieve a therapeutic level. Another option is to change the drug causing the interaction. Factors involved in evaluating drug therapy, specific to drug interactions, include appropriate management of the underlying condition, and the added expense or

References

- Anastasio GD, Cornell KO, Mescer D. Drug Interactions: Keeping it Straight. Am Fam Phy. 1997;56(3):883-8,891-4.
- Bertz RJ, Granheman GR. Use of In Vitro and In Vivo Data to Estimate the Likelihood of Metabolic Pharmacokinetic Interactions. Clin Pharmacokinet. 1997 Mar;32(3):210-58.
- Cupp MJ, Trcy TS. Cytochrome P450: New Nomenclature and Clinical Implications, Am Fam Phy. 1998;57(1):107-116.
- Jefferson JW. Drug Interactions Friend or Foe? J Clin Psych. 1998;59(suppl. 4):37-47.
- Michalets EL. Update: Clinically Significant Cytochrome P-450 Drug Interactions. Pharmacotherapy. 1998;18(1):84-112.

Tox Trivia Answers

- 1. C
- 2. b
- 3. d
- 4. a

lable 1 - Substrates, Indu	cers, and Inhibitors of the
Cytochrome P450 Isoenzy	ymes Pertinent to
Emergency Medicine	

Substrates 1A2	INDUCERS 1A2	INHIBITORS 1A2
Cyclobenzaprine Imipramine	Tobacco	Cimetidine Fluoroquinolones
Theophylline	525200	Fluvoxamine
2C9	2C9	2C9
Diclofenac	Rifampin	Amiodarone
Glipizide		Fluconazole
Ibuprofen		
Losartan		
Naproxen		
Phenytoin		
Sulfamethoxazole		
Torsemide		
warfarin	02500	102722-01215
2C19	2C19	2C19
Amitriptyline		Fluoxetine
Diazepam		Fluvoxamine
Phenytoin		Ketoconazole
2D6	2D6	2D6
Amitriptyline		Amiodarone
Clomipramine		Cimetidine
Codeine		Clomipramine
Desipramine		Fluoxetine
Flecainide		Haloperidol
Haloperidol		Methadone
Imipramine		Mibefradil
Metoprolol		Paroxetine
Propafenone		Quinidine
Thioridazine		
2E1	2E1	2E1
Acetaminophen	Ethanol	Disulfiram
Ethanol	Isoniazid	
3A4,5,7	3A4,5,7	3A4,5,7
Alprazolam	Carbamazepine	Amiodarone
Buspirone	Phenobarbital	Cimetidine
Cisapride	Phenytoin	Clarithromycin
Clarithromycin	Rifabutin	Erythromycin
Diazepam	Rifampin	Fluoxetine
Diltiazem	Troglitazone	Grapefruit juice
Erythromycin		Itraconazole
Methadone		Ketoconazole
Midazolam		Nefazodone
Quinidine		
Trazodone		
Triazolam		
Verapamil		

THE "SPI" CORNER

TOPIC: NEWSWORTHY FDA CHANGES By: Marvieen Hollenbeck, R.N. CSPI

Sildenafil citrate

In May, a recent FDA approved drug became the topic of monologues for late-night comedians. Sildenafil citrate (known to the general public as Viagra ®) became the first oral FDA-approved drug for the treatment of erectile dysfunction. Since April, an estimated 6 million prescriptions have been filled.

Sildenadil is a phosphodiesterase inhibitor. The recommended dose is 50 mg, taken approximately 1 hour prior to sexual activity. Plasma concentrations peak in approximately 30 minutes to 1 hour, however, a fatty meal will delay the peak and also decrease peak serum concentrations. The drug is metabolized in the liver, primarily by CYP 3A4 to an active metabolite. The half-life of the parent compound and the active metabolite is approximately 4 hours.

How safe is sildenafil? Adverse reactions include headache, flushing, dyspepsia, changes in color vision (a concern for pilots), diarrhea, nasal congestion, dizziness, rash and mild to moderate hypotension. When combined with organic nitrates (short or long acting), sildenafil is reported to result in potentially life-threatening hypotension and/or myocardial infarction. Other anti-hypertensives and vasodilators that do not increase nitric oxide have not shown the same effect. Other drug interactions include inhibitors of the CYP 3A4 isoenzyme (erythromycin, cimetidine, mibefradil, ketoconazole etc.), which may result in decreased metabolism of sildenafil.

The FDA has issued new warnings and the manufacturer, new labeling warning caution when prescribing sildenafil to men with coronary artery disease.

Bromfenac sodium

A third FDA change is the drug that was approved in 1997, bromfenac sodium (Duract®). Its manufacturer voluntarily withdrew it from the market in June of 1998. In February 1998, the FDA strengthened warnings on the label, re-emphasizing the duration of therapy not to exceed 10 days. However, despite the new box warning, reports of hepatic insufficiency and death continued to occur.

HOLIDAY HAZARDS

CLUES: ACROSS

- 3. Blinding toxin
- Cause of Rudolph's big eyes and red nose
- Bubble light ingredient causing CO poisoning
- New Years morning and hypoglycemia in children
- 10. Treatment is HBO
- 11. Pink berries and altered mental status
- Bacteria found in snow globes

DOWN

- 1. Non-poisonous holiday plant
- 2. Jerusalem cherry toxin
- 6. Woods lamp diagnosis
- 7. Plant causing GI upset
- 9. Antique ornament toxin

Across: 3. Methanol, 4. Anticholinergic, 5.
Methylenechloride, 8. Ethanol, 10. Carbon monoxide
11. Mistletoe, 12. Salmonella
Down: 1. Poinsettia, 2. Solanine, 6. Ethyleneglycol, 7.
Holly, 9. Lead



The CNYPCC

Toxicology Letter

Vol. IV No. 2

A Quarterly Publication

SCHEDULED EVENTS:

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

April 16, 1999 May 21, 1999 June 18, 1999

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

PROGRAM ANNOUNCEMENT:

Please mark your calendars now for the Third Annual Toxicology Teaching Day. The date has been set at the Syracuse Sheraton for November 5, 1999!

CHYPCC TIDBITS:

- Isopropyl alcohol ingestions result in ketones (in the urine and blood) without acidosis (in the blood).
- Toxin related seizures may respond better to barbiturates than phenytoin.
- Sustained Release calcium channel antagonists are the number one prescription cause of death according to the American Association of Poison Control Centers.

TOX TRIVIA:

Match the Toxin with the Organ Damaged

- 1. Phosgene
- 2. Ethylene glycol
- 3. Carbon tetrachloride
- 4. Methanol
- A. Kidney
- B. Liver
- C. Eye
- D. Lung

Case History

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

A DAY IN THE LIFE OF A POISON INFORMATION SPECIALIST (WELL. . . 10 MINUTES)

As a change of pace, we thought it would be interesting to put our readers in the position of determining the appropriate disposition of common toxin exposures. The following are examples of typical calls received by poison information specialists. Consider yourself, for the purposes of this issue, a poison information specialist and try to decide the most appropriate way to handle the following exposures:

Case 1:

The mother of a three year old female calls to report that her child has just ingested a "mouthful" of household bleach. The mother states that there is no obvious evidence of injury and that the patient has not vomited.

Sodium hypochlorite (household liquid bleach) remains a commonly used product for laundry, cleaning and disinfection. Although large amounts or high concentrations of bleach can result in burns, the vast majority of exposures do not result in significant injury. Toxic effects are a function of the concentration exposed to and contact time. Small ingestions, typical of unintentional exposures do not carry significant risk of toxicity. Therefore, aggressive evaluation is not warranted unless signs of injury are apparent such as bloody vomitus, respiratory compromise or inability to tolerate oral fluids.

Follow-up: The child was watched at home. A telephone call 30 minutes later confirmed that the child was well.

"Bleach mixing" can result in significant toxicity. The mixture of sodium hypochlorite bleach with household ammonia leads to the production of chloramine gas, a high water solubility pulmonary irritant. Toxic effects are localized to the upper airway, resulting in bronchospasm. Supportive care is usually adequate to resolve symptoms.

Mixing sodium hypochlorite with acids such as hydrochloric acid contained in toilet bowl cleaners results in the formation of chlorine gas. Chlorine gas is an intermediate water solubility pulmonary irritant. Its solubility allows it to penetrate lower into the respiratory tract before symptoms alert the patient to vacate the area. After contact with mucous membranes, hydrochloric acid is formed. Unlike dermal and mucous membrane acid exposure, the large heat exchange capacity of the lung allows the use of neutralization. Nebulized sodium bicarbonate (2%) has been used to provide symptomatic relief.

Case 2

The father of a three year old calls to report that 5 minutes ago his son has ingested one half of a small package that was in his shoe box. It is labeled silica gel - do not eat.

It is astounding how many calls are received involving silica gel. Silica gel acts as a desiccant to adsorb moisture accumulated in packaged products. Although labeling gives the impression of a toxic substance, silica gel is non toxic and this patient may be managed in the home setting without any intervention. The father receives poison prevention advice.

Case 3

A three year old female has swallowed approximately one teaspoon full of gasoline ten minutes ago. She is presently coughing and crying.

Gasoline is representative of an aliphatic (straight chain, non-substituted) hydrocarbon. Many hydrocarbon exposures result from siphoning by mouth or placement in inappropriate, attractive containers.

While most hydrocarbons are non toxic when ingested in small quantities, aspiration results in chemical pneumonitis. The American Association of Poison Control Centers reports an annual incidence of about 60,000 hydrocarbon exposures, 20 of which resulted in death. 70% of these exposures involve children, with 90% of hydrocarbon related deaths involving children <5 years of age.

Not all hydrocarbons are equal in their relative risk of being aspirated. Two important physical properties include viscosity and volatility. The less the viscosity (easier to stir) and the more the volatility, the easier it is to be aspirated. On a related note, products with low surface tension are also more likely to result in aspiration. For this reason, products such as mineral seal oil and lamp oil are much more likely to result in aspiration pneumonitis than motor oil.

After hydrocarbons are aspirated, surfactant is disrupted resulting in decreased lung elasticity. Many patients have an initial episode of coughing, gagging, and choking that occurs shortly after ingestion, usually within 10 minutes. Radiographic evidence of pulmonary injury can be delayed up to 4-6 hours after exposure. Treatment is supportive with severely poisoned patients requiring endotracheal intubation and high PEEP (positive end expiratory pressure) to maintain lung compliance. Investigational therapies include exogenous surfactant and perfluorocarbon oxygenation.

Follow-up: This patient was transported to a health care facility. After 24 hours the patient was stable, had normal pulmonary function and returned home.

Case 4

A two year old accidentally bites off the tip of a mercury thermometer and swallows the mercury. There are no cuts or bleeding noted and the child seems absolutely fine.

Poisoning with mercury can cause a multitude of systemic and local effects. However, it is important to identify the type of mercury that the patient has been exposed to in order to accurately assess risk for toxicity. The general classification of mercury products can be divided into elemental, inorganic, or organic. The mercury contained in household thermometers is elemental mercury and small quantities at room temperature do not pose a significant risk in healthy patients. However, if this type of mercury is heated while cleaning

A DAY IN THE LIFE OF A POISON INFORMATION SPECIALIST (WELL. . . 10 MINUTES)

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spills (e.g. vacuuming), vaporization can cause absorption and resultant systemic toxicity.

Patient Follow-Up: The caretaker is advised as to the proper clean up of the elemental mercury spill.

Case 5

A 20 month old male ate five of his grandfather's sublingual nitroglycerin tablets. It has been one hour and the child is asymptomatic.

Nitroglycerin is capable of causing hypotension and methemoglobinemia due to vasodilation and oxidant stress. Sublingual administration provides therapeutic effectiveness through rapid absorption directly into the blood stream. After oral administration, the combination of the inhibition of gastric absorption due to gastric pH and the fact that Nitroglycerin is extensively metabolized after the first pass through the liver, rendering it essentially non toxic.

Patient Follow-up: A telephone call 30 minutes later confirms that the child remains asymptomatic.

Case 6

A five year old boy is accidentally given two teaspoonfuls of Oil of Wintergreen (methylsalieylate) by parent. The child has slight burning in his mouth, but has not vomited.

Salicylate poisoning decreased over the past two decades after the use of aspirin products in children was associated with Reyes Syndrome. However, salicylates are still available in a variety of products including oil of wintergreen, Pepto-Bismol ®, and Alka-Seltzer ®. Aspirin is also now widely available in homes due to its use as a cardio protective agent.

Tox Trivia Answers

1. D

2. A

3. B

4. C

Clinical manifestations of salicylate poisoning include gastrointestinal upset, tinnitus, hyperventilation, diaphoresis, and hyperthermia. The mechanism of toxicity includes uncoupling of oxidative phosphorylation resulting in inefficient energy production, and eventual cellular hypoxia/death. Laboratory evaluation will often show a primary respiratory alkalosis and a primary anion gap metabolic acidosis. Significant symptoms occur after ingestion of >150 mg/kg of salicylate acutely. Less is required to cause toxic effects in patients chronically maintained on aspirin.

Methylsalicylate is a very concentrated form of salicylate. One teaspoonful contains 7.5 grams of aspirin equivalent. In a ten kilogram child (the average two year old) the minimum toxic dose (150 mg/kg) can be achieved with just over one milliliter.

Follow-up: The patient received emergent transport to a medical facility for care.

Case 7

A 14 month old girl was found nibbling on her grandmother's blood pressure medicine. One half of a clonidine 0.3 milligram tablet is missing.

Clonidine is a central alpha two adrenergic agonist. It decreases blood pressure by reducing sympathetic outflow from the central nervous system. Toxicity results in reduction in heart rate, vascular tone, and ultimately arterial blood pressure. In addition, central nervous system depression, respiratory depression, and miosis are commonly seen. Small milligram amounts have resulted in significant toxicity in children.

Follow-Up: This patient, by virtue of age criteria alone, necessitates transport to an emergency medical facility for evaluation and monitoring. Of interest, naloxone can reverse clonidine's effects in up to 50% of cases.

These are just a few examples of the typical calls received by poison information specialists at the Central New York Regional Poison Control Center.

TOPIC: ARE THEY PACKING OR STUFFING?

By: Deborah Anguish, RN, CSPI

Patient A

A young man is brought into the emergency department after attempting to evade detection of drugs he was carrying by ingesting them along with bags they were stored in.

Patient B

A woman, reported to be a heroin mule is found unresponsive with an opioid toxidrome-vital sign depression (hypotension, bradycardia, hypothermia, and hypoventilation), CNS depression, and pinpoint pupils.

Which is the stuffer and which one is a packer and why do we need to know the difference?

These patients are classified by their situation. The drugs involved are usually cocaine or heroin, and less commonly amphetamines or marijuana.

Planning and Risk for Toxicity:

The body stuffer is the patient who feels the urgent need to get rid of their drugs. Since they may not have a toilet available to flush away the evidence, they swallow it. They generally do not plan this activity and no preparations are usually made to ensure that the bags do not open. Therefore, the body stuffer is more likely to have symptoms as the bags are more likely to open, or rupture.

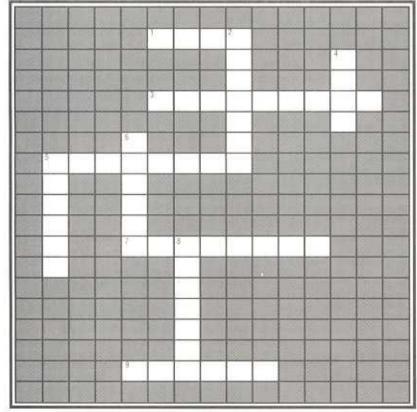
The body packer has packed for a trip, she is transporting using her GI tract. She has planned well (or more commonly, someone has planned well for her). She may have wrapped the baggies 4 thick, knowing the need to retrieve every bag, as her life may depend on handing over the exact amount of product. The packer's bags are much less likely to open. If they do open she is in grave danger, as the packers bags usually hold more and are more pure than the stuffers.

Treatment

Treatment can be complicated. The body packer that is asymptomatic needs assessment of ABC's, EKG, and abdominal X-ray (packer's bags can sometimes be visualized). Whole bowel irrigation, with some activated charcoal can help wash unopened bags out. If signs or symptoms develop in a suspected heroin ingestion titrate naloxone to protect respirations. If a packers' cocaine bags are suspected to open here, immediate surgery is required with large amounts of Benzodiazepines ready.

For the body stuffer monitor ABC's, EKG, and use multi dose activated charcoal for gastrointestinal decontamination. Treat symptoms as they arise. Use naloxone as needed for heroin. Use benzodiazepines for cocaine ingestions resulting in seizures, agitation, and hyperthermia. Avoid phenytoin, quinidine, and procainamide which may worsen toxicity.

HEAVY METALS



CLUES: ACROSS

- Most common metal associated with Metal fume fever
- 3. Mercury found in thermometers
- Hexavalent and corrosive
- 7. Painful neuropathy
- In jewelry, results in dermatitis In 10% of population

DOWN

- Pulmonary edema after inhalation.
 Osteomalacia chronically
- 4. Increased EP's and anemia
- Syndrome of CNS, liver, kidney, bone and eye damage. Also affiliated with Wilson's Disease
- Added to increase foam in beer, Resulted in cardiomyopathy, heme concentration and hyperthyroidism
- Causes alopecia and "stocking-glove" neuropathy



The CNYPCC

Toxicology Letter

Vol. IV No. 4

A Quarterly Publication

SCHEDULED EVENTS:

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

October - Canceled/Please join us at the Toxicology Teaching Day

November 19, 1999 December 17, 1999

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

PROGRAM ANNOUNCEMENT:

The Third Annual Toxicology Teaching Day is at the Syracuse Sheraton on November 5, 1999 !!! Please call 464-7078 for further information.

CHYPCC TIDBITS:

- Insulin and glucose are potential treatments for severe calcium channel antagonist toxicity.
- The pharmaceutical ketamine is knows as Vitamin K when abused as a street drug.
- Vitamin K-1 is the only acceptable vitamin K product for warfarin or super warfarin toxicity.

TOX TRIVIA:

- The toxin responsible for the most deaths according to the AAPCC in 1998 was.
- A patient after ingesting ethylene glycol exhibits an osmol gap of 20. What is the patient's minimum ethylene glycol concentration?.....
- Ethylene glycol left untreated is poisonous to this organ?

Case History

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

THE TROUBLE WITH PICNICS

Case Presentation:

Approximately eight (8) hours after enjoying a family picnic, two brothers ages 10 and 14 years were transported to the Emergency Department with complaints of fever, persistent vomiting, abdominal cramps, and diarrhea. The patients were both well before the picnic and reported no contacts with ill persons. The various foods at the family picnic included cut-up vegetables, deviled eggs, barbecued steak and chicken, cornon-the-cob, and assorted desserts. The desserts included several slices of Boston cream pie and homemade cheesecake. Liquids included kool-aid, soda, and beer. No other participants at the picnic were reportedly ill.

The patients were well throughout the day, however, upon returning home, became nauseated and dizzy. Vomiting soon began, progressing to a bilious quality. Before arriving at the hospital, both boys had several bouts of bloody diarrhea mixed with mucus.

Upon arrival in the Emergency Department both boys were ill appearing and well nourished. Blood pressure was normal without orthostatic changes. Their heart rates were elevated and their respirations were normal. Both had elevated body temperatures of 39 degrees centigrade. Head and neck examination was unremarkable. Examination of the pharynx revealed no injection. The chest was clear and the cardiac examination was normal. Both boys demonstrated voluntary guarding with hyperactive bowel sounds, but without hepatosplenomegaly. Rectal examination revealed blood and mucus. The neurological examinations were normal.

What should be considered as possible causes for this presentation of bloody diarrhea, abdominal pain, and elevated body temperature?

The initial differential diagnosis for acute diarrhea involves several idealogies: Infectious, structural, functional, toxin-induced, and food-induced.

The presence of an elevated temperature suggests the involvement of invasive organisms, including Salmonella,

THE TROUBLE WITH PICNICS (CONT.)

Shigella, Campylobacter, Escherichia coli, and Yersinia enterocolitica. Episodes of acute gastroenteritis not associated with fever are usually secondary to organisms that produce toxins, including Staphylococcus aureus, Bacillus, Clostridium, and Enterotoxigenic E. coli.

What temporal factors in the development in these illnesses are helpful in making the diagnosis?

The onset after exposure or incubation period can be useful. Extremely short incubation periods of less than six hours are typical for Staphylococcus, Bacillus and Enterotoxigenic E. coli. Intermediate incubation periods of eight to twenty-four hours are found with Clostridium, Bacillus, and Enteroinvasive E. coli, and Salmonella. Longer incubation periods are seen in other bacterial causes of acute gastroenteritis.

What measures should be undertaken within the Emergency Department?

Intravenous access should be obtained and hydration initiated immediately. In cases of abdominal tenderness, plain abdominal radiographs usually will demonstrate no abnormal findings. Complete blood counts should be obtained in all patients with the suspicion of infectious diarrhea. Electrolyte determination should be measured as well.

A gram stain of the stool should be obtained to demonstrate the presence or absence of Polymorphonuclear cells.

What epidemiologic factors can assist in the diagnosis?

It is important to establish the presence of an epidemic occurrence in cases of bloody diarrhea. The presence of two (2) or more cases strongly supports the possibility of food born diseases. The concurrent symptomology supports this as well. Both patients became ill at approximately the same time and it is more than likely that food was the culprit. It is often quite difficult to determine which foods were served and to whom, however, both of these children admitted to eating egg salad, both meats, and all desserts.

In our cases, it seems most likely that the lengthy incubation period (8 hours) effectively rules out most non-bacterial idealogies, and toxin producing organisms.

When analyzing the potential causative food groups at this picnic, it is important to consider the risk of Staphylococcal food poisoning. Foods that are inadequately cooked or are allowed to either get warm or sit for prolonged periods of time, especially dairy and poultry products may prove to be harmful when ingested. Specific foods to consider as potential Staphylococcal entities include milk products and other proteinaceous foods, creamfilled baked goods, potato & chicken salads, sausages, ham, and gravy. At this picnic, poultry, cream pie, and potato salad were considered to be suspicious by the clinicians. It is important to recognize that all pies that contain thick crusts. which can potentiate the development of toxin production even during refrigeration. Here, the crust acts as an insulator maintaining the internal temperature of the cream filling. After a detailed history was taken, it became obvious that our two victims had been the only picnic participants that had ingested the Boston cream pie.

Specific Organisms Related to Food Born Illness Staphylococcus

Patients with Staphylococcus food poisoning may either present with or without fever. Abdominal pain, nausea followed by vomiting and diarrhea dominates clinical picture. The mean incubation period in most cases is 4.4 hours with a mean duration of illness of twenty hours.

Food sources of Staphylococcus include prepared foods, meats, pastries, and salads.

Salmonella species

Salmonella infections have become a great concern in the United States. People who consume raw or undercooked eggs are most at risk for Salmonella enteritis. Typically, raw eggs may be found as ingredients in chocolate mousse, hollandaise sauce, eggnog, caesar salads, and homemade ice cream. Whole, partially cooked eggs may be eaten as sunny side up or poached. There has been additional concern developing over the wide spread use of antibiotics in animal feed. Meats and poultry now frequently contain resistant bacterial strains that place virtually any population at risk.

Campylobacter jejuni

Campylobacter jejuni is a major cause of bacterial enteritis. It is most commonly isolated in children younger than five years of age and adults twenty to forty years of age. Outbreaks are more common in

THE TROUBLE WITH PICNICS

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the summer months. Outbreaks are associated with contaminated food or water. The most frequent sources are unpasteurized milk and raw or undercooked poultry products. Birds are a common source. The organism is heat labile and cooking will often prevent human transmission. The incubation period for Campylobacter varies from 1 to 7 days. The illness may last from 5 – 6 days. Treatment is supportive with volume resuscitation. Oral Erythromycin decreases fecal shedding of the organism.

Yersinia enterocolitica

Yersinia enterocolitica is an organism that causes enteritis most frequently in children and young adults. Patients will typically complain of fever, abdominal pain and diarrhea, which usually contain blood and mucus. The incubation period may be one day to one week or more. Less common features include prolonged diarrhea, arthritis, and liver enlargement. Sources of human infection

include milk products, raw pork, person-to-person transmission, and rarely as a side effect of deferoxamine antidote treatment (for iron poisoning). Therapy is supportive; however, patients with invasive disease should be treated with intravenous antibiotics, specifically third generation Cephalosporins.

Case Development

Within the Emergency Department, both patients rapidly improved with intravenous rehydration. Both patients demonstrated elevated white counts with a left shift. Electrolytes were normal. Abdominal films ruled out the presence of ileus or obstruction. Both stools were positive for the presence of fecal leukocytes. On the basis of the time of presentation and the exposure to dairy products, the diagnosis of Staphylococcal induced food poisoning was entertained. Both patients were admitted overnight to the hospital and stool cultures were positive for Salmonella species. Both patients recovered uneventfully.

THE "SPI" CORNER

TOPIC: BOTULISM

By: T. Michele Caliva, R.N., CSPI

A 44-year old female presents to the Emergency Department with anticholinergic symptoms, sore throat, diplopia, and descending paralysis. Family members stated that the previous day she had GI symptoms including nausea, vomiting and abdominal pain.

This scenario is one of the most difficult cases to diagnose and treat. Conditions to consider in the differential may include Encephalitis, Tetanus, MS, Myasthenia gravis, Guillain-Barré along with many viral or bacterial causes. In addition several toxicological causes such as an exposure to heavy metals, plants, mushrooms, tick bite, snake bite, paralytic shellfish poisoning and food poisonings should be considered.

Tox Trivia Answers

- tricyclic antidepressants
- normal osmol gap is (-14-+10). This patient is +10 at least. Last part of calculated osmol gap equation is alcohol/# = gap... In this patient X/6.2 = 10, level = at least 62 mg/dL.
- Kidneys

A history taken from this patient revealed that she developed gastrointestinal symptoms a few hours after ingesting home canned peaches. Any patient that presents with these types of symptoms and admits to ingesting home canned products should be evaluated for botulism toxicity. Botulism toxin is a protein with a toxic and non-toxic component. This protein binds irreversibly to the cell membrane where it inhibits the release of acetylcholine presynaptically. The end result is descending paralysis.

There are six recognized classes of botulism: C. botulism- types A, B, E, infant botulism, adult type infant botulism and wound botulism. Types A, B, and E are associated with food borne exposures to pre-formed toxin, whereas wound botulism is caused when an open sore/wound is exposed to contaminated soil. Infant botulism and adult type infant botulism occur when patients are exposed to C. botulism in the gastrointestinal tract and are unable due to relative achlorhydria, to destroy the bacteria, thereby allowing toxin to be generated. This has historically been associated with naturally occurring honey in children under the age of 1 years of age.

THE "SPI" CORNER - TOPIC: BOTULISM (CONT.)

The diagnosis of botulism can be confirmed through analysis of stool, the wound or suspected food. Electromyography may also be used to help make the diagnosis.

Symptoms of botulism toxicity usually begin within a few hours of ingesting the contaminated food. Nausea, vomiting and abdominal discomfort predominate early, followed by throat pain, visual changes such as diplopia, fixed pupils, urinary retention and descending paralysis. Finally, symptoms progress to include total respiratory compromise.

The effectiveness of treatment of botulism poisoning is linked to how quickly the patient

receives treatment. Respiratory support is imperative and activated charcoal should be considered in cases of ingestion. The antidote, botulism antitoxin is useful to prevent further progression of symptoms.

Prevention of food borne botulism requires identification and avoidance of conditions favorable for spore growth including; a temperature on or below 100 degrees centigrade, a climate with a low percentage of sodium chloride and nitrates and a pH over 4.5.

SUBSTANCES NOT ADSORBED TO ACTIVATED CHARCOAL

CLUES: ACROSS

- 1. Garlic Smell
- Paint Chips, Curtain Weights and Sinkers
- Found in Prenatal Vitamins
- 6. Gasoline and Lamp Oil
- Methanol and Ethylene Glycol

DOWN

- 2. Toilet Bowl Cleaners
- Dietary Supplement,
 Some Forms are
 Caustic
- Metal Used for Manic Depressive Illness
- Found in Vicks® Vaporub

Across: 1, Arsenic, 4 Lead, 5, Iron, 6, Hydrocarbons, 8. Alcohols Down: 2, Caustics, 3, Zinc, 4, Lithium, 7, Camphor