Pediatric Toxicology
Small Doses = Big problems

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Objective

- **When to be concerned about a curious toddler who ingests 1-2 tablets or swallows of a medication or household product**

Background

Age two children have motor independence

Injury Hospitalizations in Virginia - 2007

Epidemiology

(AAPCC.org)

American Association of Poison Control Centers

2008 Poisoning Fatalities

Poisoning Fatalities

Pediatric Poisoning Fatalities - 2008

- Age < 6 yrs: 2% of all fatalities
- 0.002% of pediatric exposures
- Carbon monoxide / smoke inhalation
- Narcotics (oxycodone)
- Scorpion sting
- Tetrodotoxin food poisoning
- Inhalants

Fatalities by Reason & Age

“Pill Can Kill”

Relevant Articles

1 Commercially Available Dose Can be Potentially Fatal to 10 kg Toddler

- Camphor
- Chloroquine, quinine
- Cyclic antidepressants
- Phenothiazines
- Methyl salicylate
- Theophylline

Other Products in Which One Dose can be Toxic to a Toddler

- Clonidine (imidazolines)
- Lomotil®
- Antifreeze (ethylene glycol)
- Alcohols
- Sulfonylureas
- Caustics
- Hydrocarbons

Case

- **A 9-month-old infant is inadvertently fed 2-3 teaspoonfuls of crystals from a Drano container. What steps should be taken to decontaminate the child?**

Alkaline Corrosives

- Immediate airway concern
- Liquefaction necrosis
- Liquid or solid product?
- Lack of oral burns can be misleading
- Vomiting, drooling, stridor
- Supportive care

- **NO ipecac or gastric lavage**

Petroleum Distillates

- **Gasoline**
- **Kerosene**
- **Lamp oil**
- **Lighter fluid**
- **Liquid polish**

Petroleum Distillates

- Risk for aspiration – related to viscosity
- Chemical pneumonitis
- Symptoms within 6 hours
- Supportive pulmonary toilet
- No role for steroids or antibiotics
- DO NOT induce emesis (ipecac)!

Products with Camphor

Camphorated oil	**23%**
Campho-Phenique	**10.8%**
Camphor spirits NF	**10%**
Soltice Quick Rub	**5%**
Soltice Quick Rub Childrens	**3.75%**
Vicks Vaporub	**4.8%**
Ben-gay ultra strength	**4%**

Camphor Toxicity

- **Lipophilic cyclic terpene with CNS stimulant properties**
- **Antipruritic, rubefacient, antiseptic**
- **Oral and throat irritation**

- **Nausea and vomiting**
- **Confusion, restlessness, seizures**
- **Onset 5-15 minutes**

Camphor

Camphor Toxicity

- **1 g has caused death in a chilld**
- **2 g causes significant adult toxicity**
- **Clinically significant toxicity does not occur with < 30 mg/kg and is rare with doses < 50 mg/kg (Geller et al, 1984)**
- **Refer to HCF for ingestions > 500 mg**
- **Avoid milk or fatty foods**

Mothballs

- **Naphthalene**
- **Paradichlorobenzene**
- **Camphor**

- **Also found in cake deodorizers (diaper pale, toilet bowl)**
- **Toxicity: seizures, hemolysis, methemoglobinemia**

Mothball Ingestion

- **A 7 year-old girl bit into 2 mothballs thinking they were candy – only small amount believed swallowed**
- **PMH of developmental delay, CVA**
- **3 days later presented to ED with dark urine and scleral icterus**
  - **Acute hemolysis: Hgb 7 (nl 12)**
  - **Methemoglobinemia: 4.4%**
  - **Total bilirubin 7.8**

Naphthalene-Induced Hemolysis

- Naphthalene epoxide metabolite causes oxidative stress
- RBC glutathione is reduced in pts with G-6-PD deficiency

Methanol

- Sources: gasoline antifreeze, windshield washer fluid, sterno
- Inebriation, lethargy, coma
- Blurred vision → blindness; retinal edema, hyperemia
- Metabolic acidosis
  (delayed: 18-24 h)

Methanol Metabolism

Methanol

- Rapid decontamination
- Check methanol blood level, serum osmolality
- Folic acid / leucovorin
- Inhibit MEOH metabolism:
  - Ethyl alcohol – intravenous
  - 4-methylpyrazole (Antizol®)
- Hemodialysis
  - Based on symptoms, acidosis, level

Sulfonylureas

- Stimulate insulin secretion
- Increased insulin responsiveness
- Onset of hypoglycemia may be delayed for 8-12 hours
- Treatment with IV dextrose usually is sufficient
- Other Tx: diazoxide, glucagon, octreotide

Sulfonylureas

- Chlorpropamide:
  - A 9-year-old male ingested 5 g chlorpropamide. He was comatose 24 hours post-ingestion, and had seizures despite intensive dextrose treatment.

- Glipizide:
  - A two-year-old child developed delayed hypoglycemia 11 hours after ingesting 1 glipizide 5 mg tablet and 1 hydrochlorothiazide 25 mg tablet. BG was 49 mg%.

Glyburide

- A 22-month-old boy ingested one 5mg tablet. His BG was 64 mg% at 2.5 hours post exposure.

- A 20-month-old boy ingested 15 mg. He was admitted 21 hours postingestion with somnolence, seizures, and a BG of 52 mg/dL. A protracted course ensued, with coma lasting 4 days. Residual effects included optic nerve atrophy, seizures, and developmental retardation.

Octreotide for Refractory Hypoglycemia

Other Hypoglycemics

- **Metformin:**
  - In a series of 46 cases (dose ranged from 250 mg to 16.5 g) in children, no patient experienced hypoglycemia or lactic acidosis (Spiller et al, 1999).

- **Glitazones:**
  - Limited overdose data. Hypoglycemia rarely occurs with therapeutic doses.

Clonidine

- Centrally acting alpha agonist that reduces sympathetic tone
- Results in reduced BP (reduced PVR) and decreased HR (increased vagal)

- Toxic effects: CNS depression, respiratory depression, bradycardia, hypotension, miosis, hypothermia

Clonidine Toxicity

- Clinically resembles opioid toxicity
- Onset within 1-2 hours

- Treatment is largely supportive
- Naloxone – may require higher doses

Other Imidazolines

- **Antihypertensives:**
  - **Guanfacine (Tenex)**
  - **Guanabenz (Wytensin)**

- **Decongestants**
  - **Tetrahydrozoline (Visine)**
  - **Oxymetazoline (Afrin)**
  - **Naphazoline (Clear Eyes)**

Lomotil

- **Diphenoxylate 2.5mg + atropine 0.025mg**

- **Lethargy reported after ingestion of 1 tablet**
- **CNS depression may be delayed up to 18 hours**

- **Treatment is supportive**
  - **Naloxone for opiate effects**
  - **Physostigmine has been used for anticholinergic toxicity**

Methyl Salicylate

- **1 cc of 98% = 1,400 mg aspirin**
- **One swallow (5 ml) is equivalent to 7 g of aspirin, which = 466 mg/kg in a 15 kg child.**
- **Ingredient in Wintergreen alcohols and topical analgesics (15-30%)**
  - **Ben-Gay**
  - **Icy Hot**

Salicylate Toxicity

- **GI irritation – N/V/D, abdominal pain**
- **Tinnitus**
- **CNS stimulant – hyperventilation, agitation, seizures, coma**
- **Hypoglycemia**
- **Metabolic acidosis, hyperthermia**
- **Pulmonary edema**
- **Coagulopathy**

Salicylate Treatment

- **Activated charcoal**
- **Serial salicylate levels, BMP, ABG**
- **Urinary alkalinization (pH 7.5 – 8.0)**
- **Hemodialysis**
  - **Significant altered mental status**
  - **Refractory acidosis**
  - **Renal failure**
  - **Serum level – acute or chronic?**

Amanita Phalloides

Amanita Phalloides

- **“Death Cap”, “Destroying Angel”**

- **Amatoxins inhibit RNA polymerase II**

- **Onset of (severe) GI distress 6-12 hours following ingestion**

- **Central zonal hepatocellular necrosis peaks 72 hours post ingestion**

Amanita Phalloides Poisoning

- **A 3-year-old girl presented with abdominal pain, vomiting & diarrhea**
- **AST 16,648; ALT 9,844; TB 23 mg%**
- **PT 34.2 sec**
- **Grade III encephalopathy**
- **Orthotopic liver transplant on day 5**
- **Survived with neurologic impairment**

Amanita Treatment

- **Activated charcoal – MODAC**
- **Charcoal hemoperfusion**
- **Monitor for liver failure**
- **Transplantation**

- **Experimental therapy:**
  - **Penicillin G (300,000 – 1,000,000 u/kg/d)**
  - **Silibinin (20-50 mg/kg/d)**
  - **Thioctic acid (50-150 mg q 6 hrs)**
  - **Cimetidine**
  - **N-acetylcysteine**

Ethylene Glycol

- Radiator antifreeze
- Estimated lethal dose = 100 ml (1.4 ml/kg)
- Clinical effects:
  - Neurologic (0.5 – 12 hrs)
  - Cardiopulmonary (12-24 hrs)
  - Renal (24-72 hrs)

Ethylene Glycol

- **Rapid decontamination**
- **Check osmolality – EG blood level**
- **Check for crystalluria**
- **Thiamine / pyridoxine**
- **Inhibit MEOH metabolism:**
  - **Ethyl alcohol – intravenous**
  - **4-methylpyrazole (Antizol®)**
- **Hemodialysis**
  - **Based on symptoms, acidosis, level**

Hydrofluoric Acid

- A healthy 12-month-old girl was playing in her walker when a bottle of glass etching cream fell onto the walker tray
- Mother noticed the product on the child's hands and placing her hands in her mouth
- Vomiting was induced and the child became sleepy
- The child arrived at MCV 2 hrs later

Hydrofluoric Acid

- On ED arrival: child was in no distress and acting appropriate for her age
- P/E: crying, tachycardic (188), no lesions

- Dermal decontamination and PO calcium given
- Serum Ca = 6.8 mmol/L (9.1-10.9)
- Ca(i) = 0.96 mmol/L (1.16 – 1.32)
- CO_2 = 15 mmol/L (21-33)
- EKG: sinus tach (175), PR 94, QRS 54, QTc 436
- IV calcium 1g infusion

Hydrofluoric Acid

- ED: noted to playful and alert – fell asleep during calcium infusion
- Sudden onset of jerking movements
- Unresponsive, torsades de pointe on monitor
- CPR, Mg, Ca, Epi, defibrillation
- Child died about 4.5 hours after exposure
- Autopsy – normal, no oral or dermal lesions

Household Hydrofluoride Products

- Glass Etching Creams
  - Ammonium bifluoride 60%

- Rust Removers / Wheel Cleaners
  - Hydrofluoric acid 10-12 %

Chloroquine

- **Blocks enzymatic synthesis of RNA and DNA**
- **Quinidine-like effects on the heart**
  - **Impaired conduction & contractility**
- **Half-life = 1-60 days**
- **In children, doses 2-3 x greater than therapeutic (< 1 gm) have been fatal within 2-3 hrs**

Chloroquine Toxicity

- **Hypotension, shock**
- **Bradycardia or tachycardia**
- **Conduction (QRS) delay**
- **Agitation, CNS depression**
- **Hypokalemia**

- **Cardio-respiratory arrest**

Chloroquine Treatment

- **Early intubation**
- **Epinephrine titrated to hypotension**
- **Diazepam for agitation, seizures, cardiotoxicity (may compete for binding sites)**
- **Na bicarbonate**
- **Cautious replacement of K^+**

Lindane

- Multiple cases of seizures following single dermal applications or accidental ingestion
- Onset often within 15-30 minutes
- Some cases had coma & respiratory depression
- Nausea and vomiting is common
- Refer all cases to ED
- An organochlorine insecticide that interferes with Na and K transport, and indirectly inhibits GABA

Methemoglobinemia

- Benzocaine, lidocaine
- Aniline dyes
- Naphthalene
- Phenazopyridine
- Nitrites, nitrates
- Chlorates

Methemoglobinemia

- **Oxidized Hgb does not carry or deliver oxygen**

- **Dyspnea, chest pain, CNS symptoms**
- **Chocolate brown colored blood and cyanosis unresponsive to O_2**

therapy

Methemoglobinemia

- **< 15% Asymptomatic**
- **15-30% Cyanosis**
- **30-55% Headache, fatigue, dizzy, tachycardia, lethargy**
- **55-70% Coma, acidosis, seizures, dysrhythmias**

Methemoglobinemia

Methemoglobinemia

- **Management = reduction of metHgb with methylene blue**
- **1-2 mg/kg (0.1-0.2 ml/kg) of 1%**
- **May repeat at 1 hr intervals**
- **Avoid doses > 7 mg/kg**

Sudden Sniffing Death

- Onset in minutes
- Unpredictable
- Combination of low oxygen and cardiac rhythm disturbance
- Victims usually found unresponsive (dead)
- Resuscitation unlikely

What are Inhalants?

- Paint thinner and other solvents
- Nail polish remover
- Fuel vapors
- Propellants (aerosols)
- Glues
- Refrigerants
- Anesthetics (nitrous oxide)
- Nitrites (poppers, room odorizers)
- Butane (cigarette lighters)

Sudden Sniffing Death

- 39 deaths reported in Virginia, 1987-1996
- Mean age: 19
- 46% involved butane or propane

- 144 deaths reported in Texas, 1988-1998
- Mean age: 24
- 35% involved refrigerants (Freon)

Stages of Intoxication

Symptoms of Inhalant Abuse:

Acute Medical Problems

- Euphoria, loss of consciousness
  - Brain is not getting enough oxygen
- Irregular heart beat
  - Stress hormones are circulating at high levels
  - Affect electrical conduction in the heart
- Frostbite
- Trauma
- Suffocation

Post-lecture Questions

All of the following contain methylsalicylate except

- Oil of wintergreen
- Ben Gay ointment
- Icy Hot ointment
- Campho-phenique

Imidazolines are similar to what antihypertensive agent

- Beta blockers
- Clonidine
- Calcium channel blockers
- Ace inhibitors

Toxicity of camphor is primarily:

- Hepatic injury
- Metabolic acidosis
- Seizures
- Cardiac arrhythmias

Benzocaine exposure may result in:

- Coma
- Urinary retention
- Hypotension
- Methemoglobinemia

What toxidrome may be seen with Lomotil ingestion?

- Sympathomimetic
- Anticholinergic
- Cholinergic
- Opioid

Summary

- Be aware of these chemicals
  - Methyl Salicylate
  - Camphor
  - Imidazolines
  - Sulfonylureas
  - Benzocaine
  - Lomotil
  - Quinine
  - Ethylene glycol
  - Methanol

Methemoglobinemia

Methemoglobinemia

- **Infants:**
  - **Fetal Hgb more susceptible to oxidation**
  - **High gastric pH → growth of nitrate reducing bacteria → increased nitrite**
  - **Transient deficiency of NADH-dependent methemoglobin reductase – up to about 4 months of age**

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