

Pediatric Toxicology

Small Doses = Big problems

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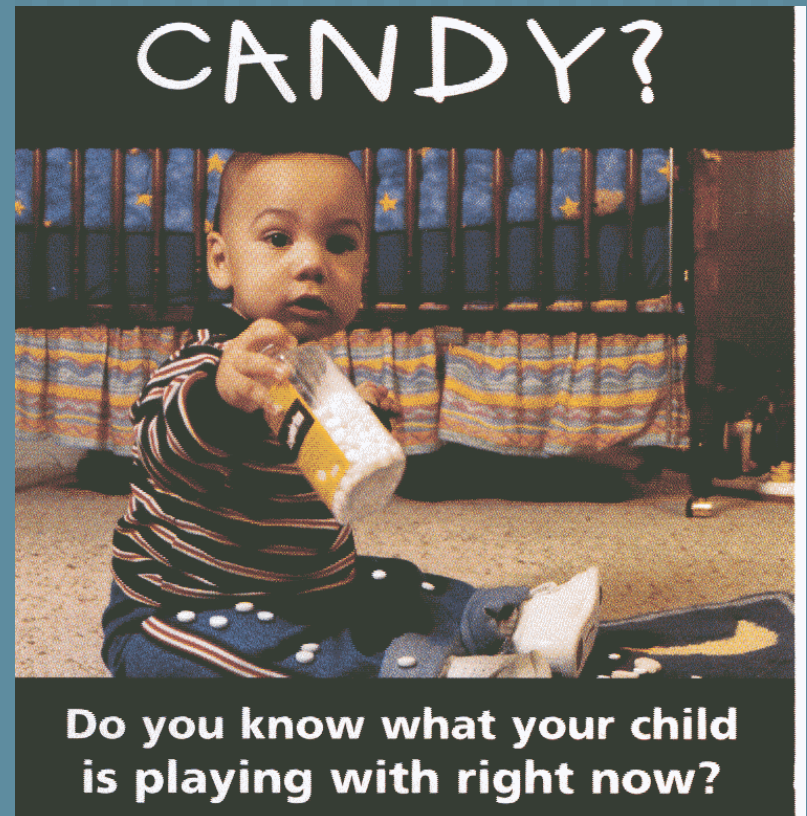
Objective



- **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



Do you know what your child is playing with right now?



Injury Hospitalizations in Virginia - 2007

CAUSE	# of Discharges	%	Total Charges
Falls	18,671	44	\$ 495 M
Poisoning	6,607	16	\$ 82 M
MVA occupant	3,259	7.7	\$ 125 M
Unspecified	2,307	5.5	\$ 53 M
Cut / pierce	1,629	3.9	\$ 251 M

Epidemiology

(AAPCC.org)

AAPCC NPDS data

- Average total exposures: 2,195,164
- Average pediatric exposures: 1,301,894
- Average pediatric fatalities: 31

American Association of Poison Control Centers

TABLE 17B. Substances Most Frequently Involved in Pediatric Exposures (Children Under 6 Years)

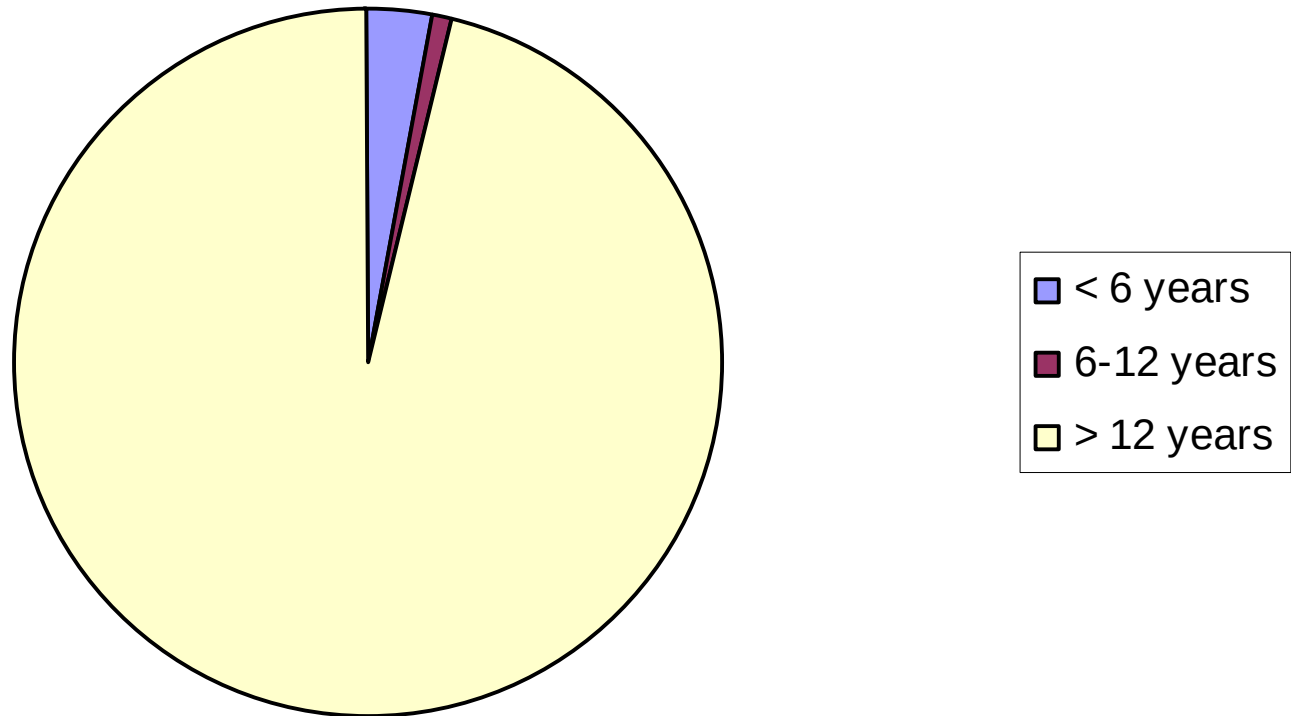
Substance	No.	%*
Cosmetics and personal care products	166,874	13.4
Cleaning substances	121,048	9.7
Analgesics	97,463	7.8
Foreign bodies	92,166	7.4
Topicals	92,091	7.4
Cough and cold preparations	68,493	5.5
Plants	57,778	4.6
Pesticides	50,938	4.1
Vitamins	45,352	3.6
Antimicrobials	35,152	2.8
Antihistamines	32,622	2.6
Arts/crafts/office supplies	31,211	2.5
Gastrointestinal preparations	29,770	2.4
Hormones and hormone antagonists	23,787	1.9
Electrolytes and Minerals	22,337	1.8

2008 Poisoning Fatalities

Substance	All mentions	All mentions %	# of Single Exposures	Single Exposures %
Sedative / Hypnotics / Antipsychotics	467	14.81	32	3.96
Opioids	401	12.72	66	8.17
Antidepressants	247	7.83	29	3.59
Cardiovascular Drugs	238	7.55	54	6.68
Acetaminophen Combinations	235	7.45	53	6.56
Alcohols	210	6.66	40	4.95
Stimulants and Street Drugs	184	5.84	53	6.56
Acetaminophen Alone	168	5.33	69	8.54
Antihistamines	98	3.11	6	0.74
Anticonvulsants	85	2.7	4	0.5
Muscle Relaxants	83	2.63	6	0.74
Fumes / Gases / Vapors	78	2.47	63	7.8
Acetylsalicylic Acid Alone	73	2.32	25	3.09
Cyclic Antidepressants	71	2.25	17	2.1

Poisoning Fatalities

Fatalities by age



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

Age	N	Suicide	Accident	Sub Abuse	Drug Error	Environ	Unk	Fetal	Malicious
< 1 yrs	8		3		2			2	1
1 - 5 yrs	18		12		5	1			
6 - 12 yrs	12		2	1	1	4	4		
13 - 17 yrs	42	22	3	11	2	2	2		
TOTAL	80	22	20	12	10	7	6	2	1

AAPCC, 2002.

“Pill Can Kill”

Relevant Articles

Medication Which Can Kill a Toddler With One Tablet or Teaspoonful.

Koren G. *Clin Toxicol* 1993;31(3): 407-413.

Small Doses, Big Problems: A Selected Review of Highly Toxic Common Medications.

Liebelt, Shannon. *Pediatr Emerg Care* 1993; 9(5):292-297.

Deadly Pediatric Poisons: nine common agents that can kill at low doses.

Michael, Joshua. *Emerg Med Clin N Amer* 2004; 22:1019-1050.

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

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

Koren G, Clin Toxicol 1993; 31:407-13.

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**

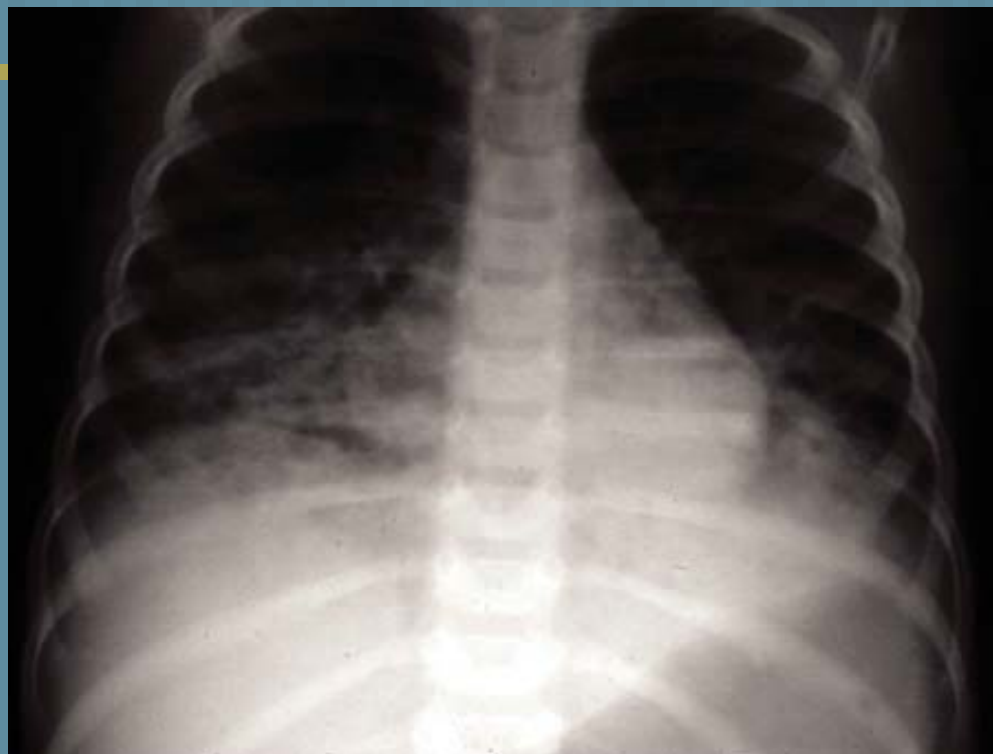
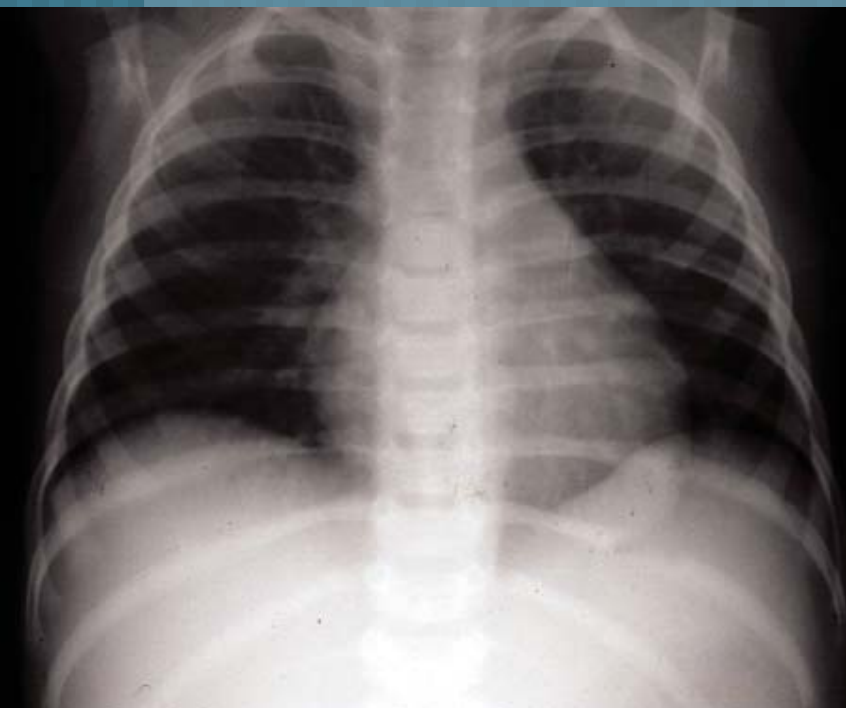
Petroleum Distillates

- 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)!



Chemical Pneumonitis

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 %



Camphorate Oil

KEEP THIS AND ALL OILS
OUT OF REACH OF CHILDREN
IN CASE OF ACCIDENT
OR FIRE, CALL FIRE
DEPARTMENT
FOR ASSISTANCE
A. P. L. CO. CO. CO. CO.
MADE IN U.S.A.

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

- Cyclic ketone of aromatic terpene group
- Lipophilic with excitatory and inhibitory effects
- Lethal dose = 50-500 mg/kg
- 5cc (1gram) caused death in 19 month old

= 10 cc Campho-phenique
= 16 cc Vicks Vapo-steam
= 20 cc Vicks Vapo-rub



Camphor Toxicity

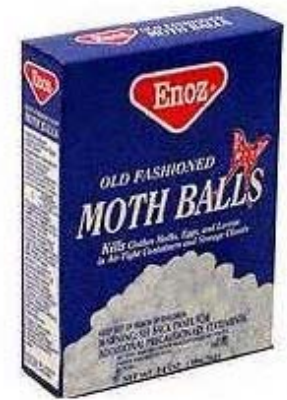
- 1 g has caused death in a child
- 2 g causes significant adult toxicity
- Clinically significant toxicity does not occur with < 30 mg/kg and is rare with doses < 50 mg/kg (Geller et al, 1984)
- Refer to HCF for ingestions > 500 mg
- Avoid milk or fatty foods

Mothballs

- Naphthalene
 - Paradichlorobenzene
 - Camphor
-
- Also found in cake deodorizers (diaper pail, toilet bowl)
 - Toxicity: seizures, hemolysis, methemoglobinemia

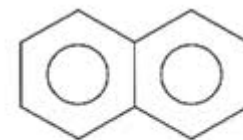


Mothball Ingestion



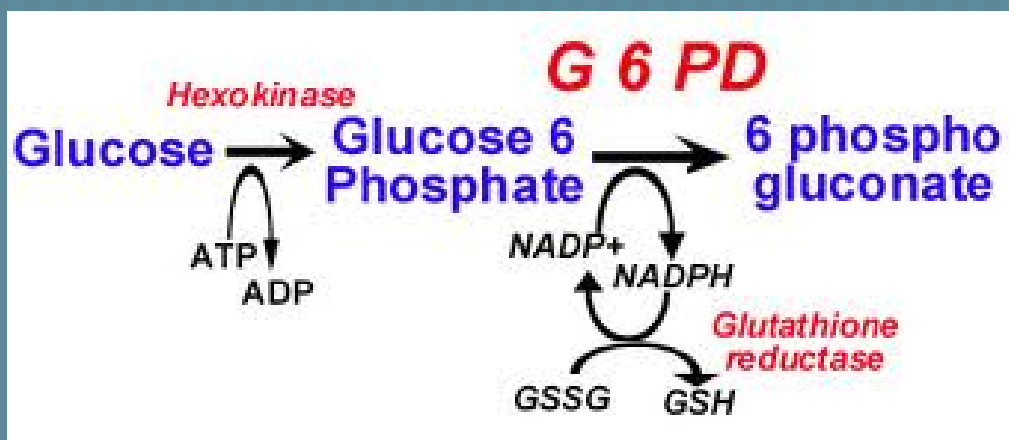
- A 7 year-old girl bit into 2 mothballs thinking they were candy – only small amount believed swallowed
- PMH of developmental delay, CVA
- 3 days later presented to ED with dark urine and scleral icterus
 - Acute hemolysis: Hgb 7 (nl 12)
 - Methemoglobinemia: 4.4 %
 - Total bilirubin 7.8

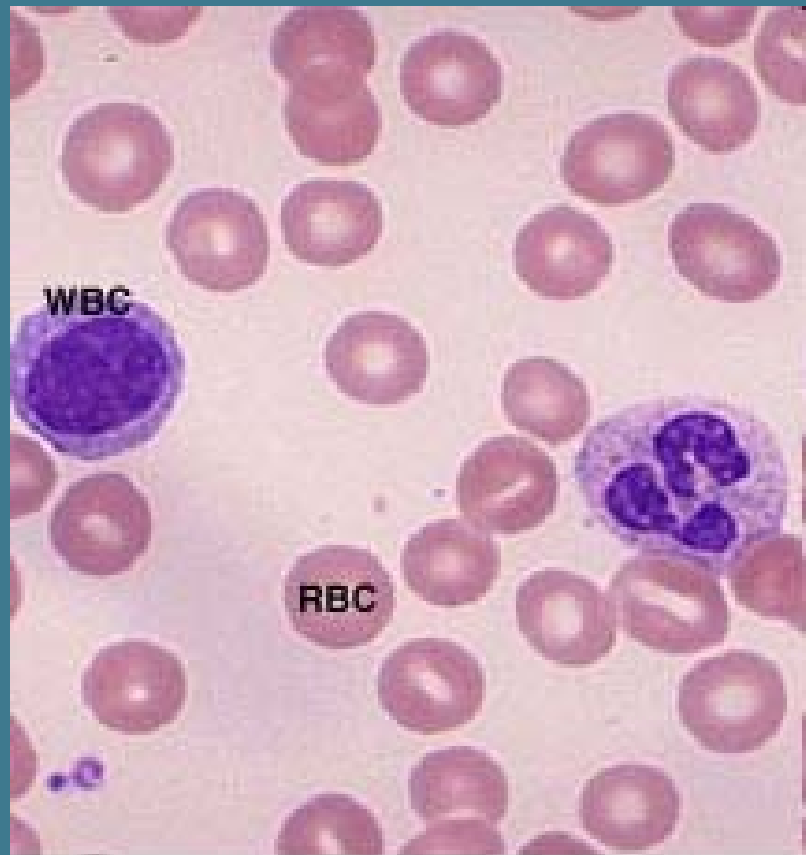
Naphthalene-Induced Hemolysis



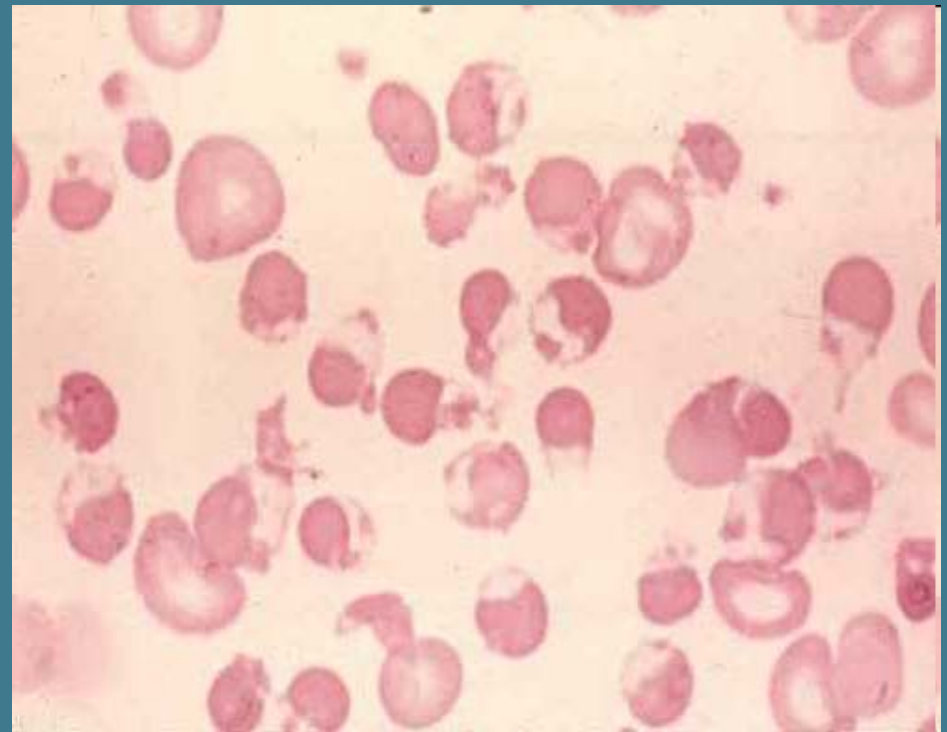
Naphthalene
 $C_{10}H_8$

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





Normal Blood Smear



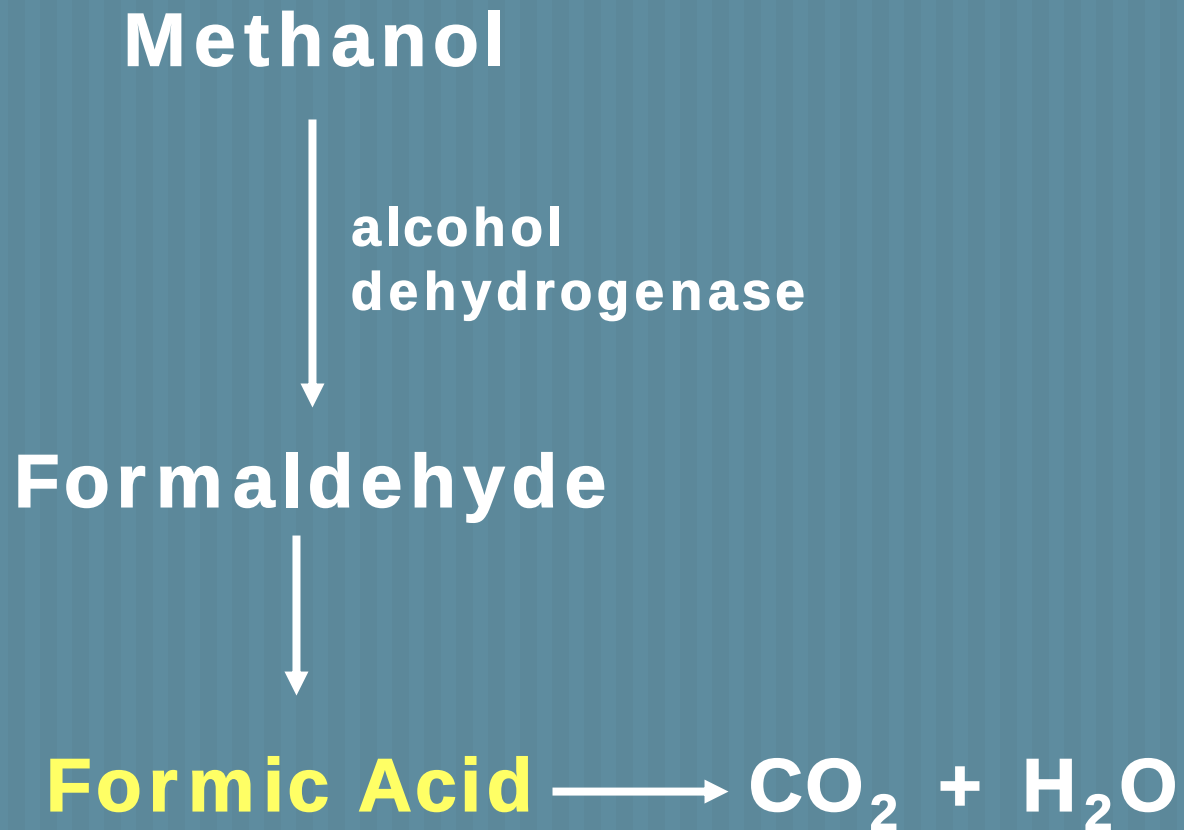


Methanol

- 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

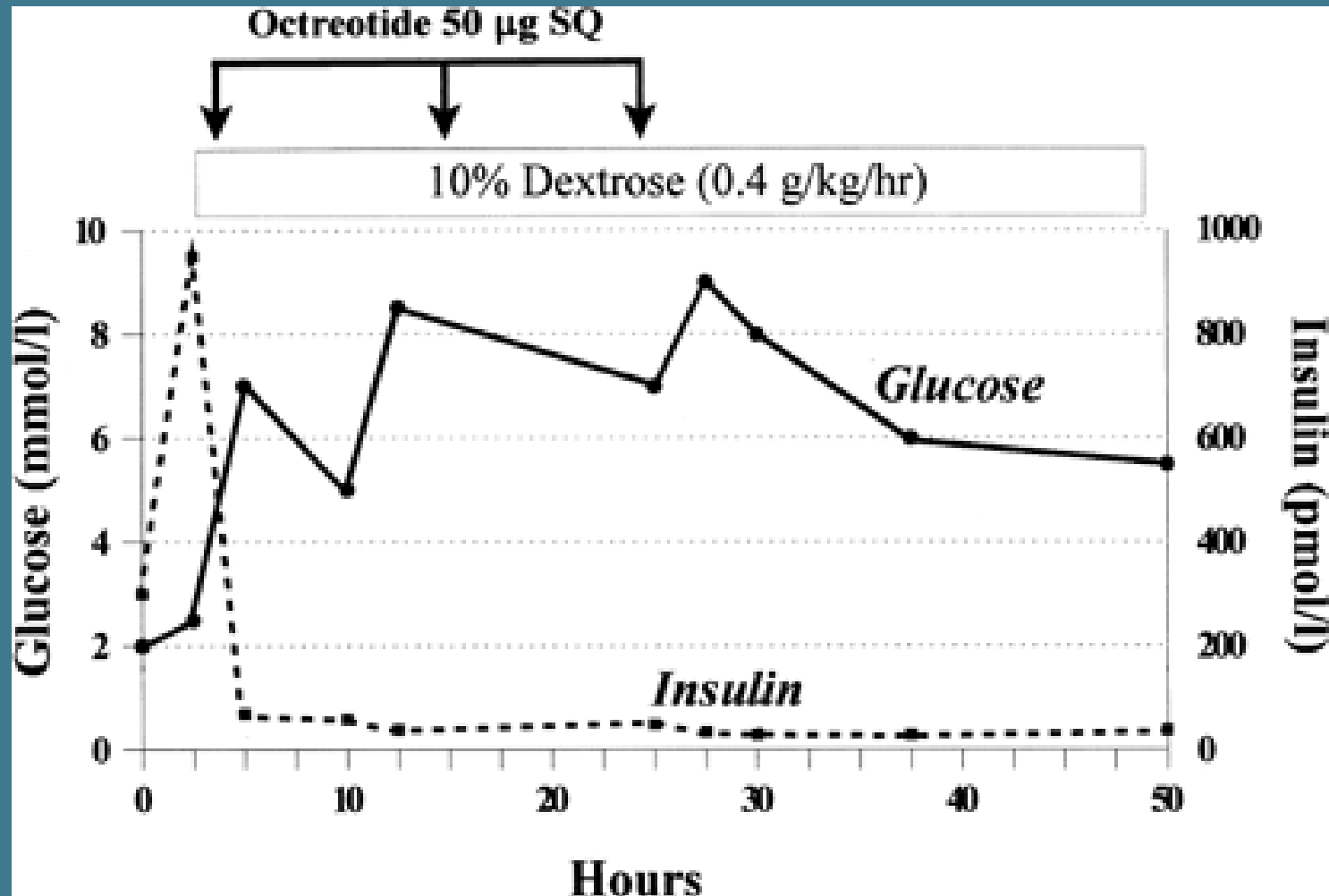
Sulfonylureas

- **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



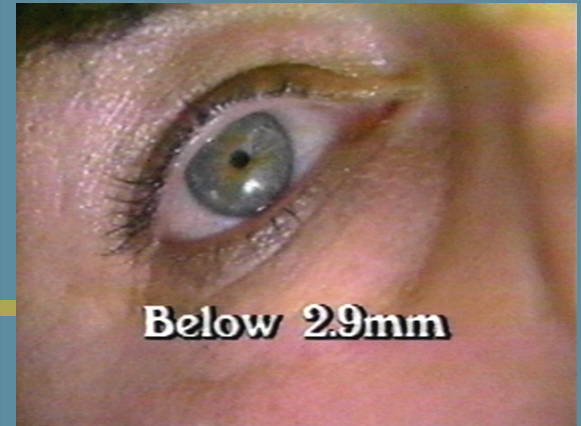
Other Hypoglycemics

- **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 alkalization (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

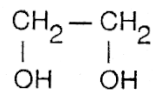
Amanita Treatment

- **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**

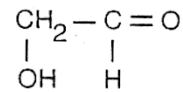
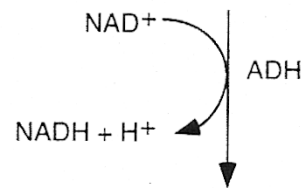
Ethylene Glycol

- 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)

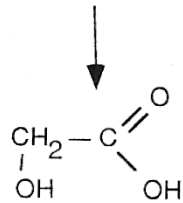




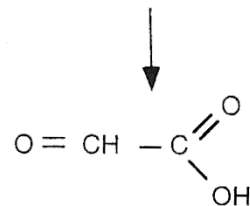
ETHYLENE GLYCOL



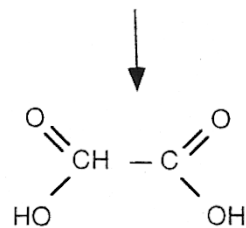
GLYCOALDEHYDE



GLYCOLIC ACID



GLYOXYLIC ACID



OXALIC ACID

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

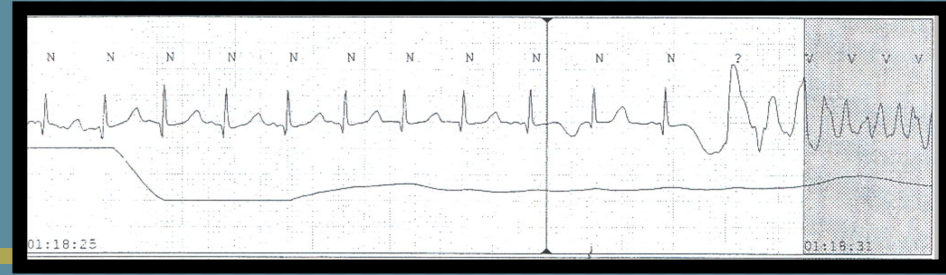
- A healthy 12-month-old girl was playing in her walker when a bottle of glass etching cream fell onto the walker tray
- Mother noticed the product on the child's hands and placing her hands in her mouth
- Vomiting was induced and the child became sleepy
- The child arrived at MCV 2 hrs later



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)
- CO₂ = 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 pointes 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

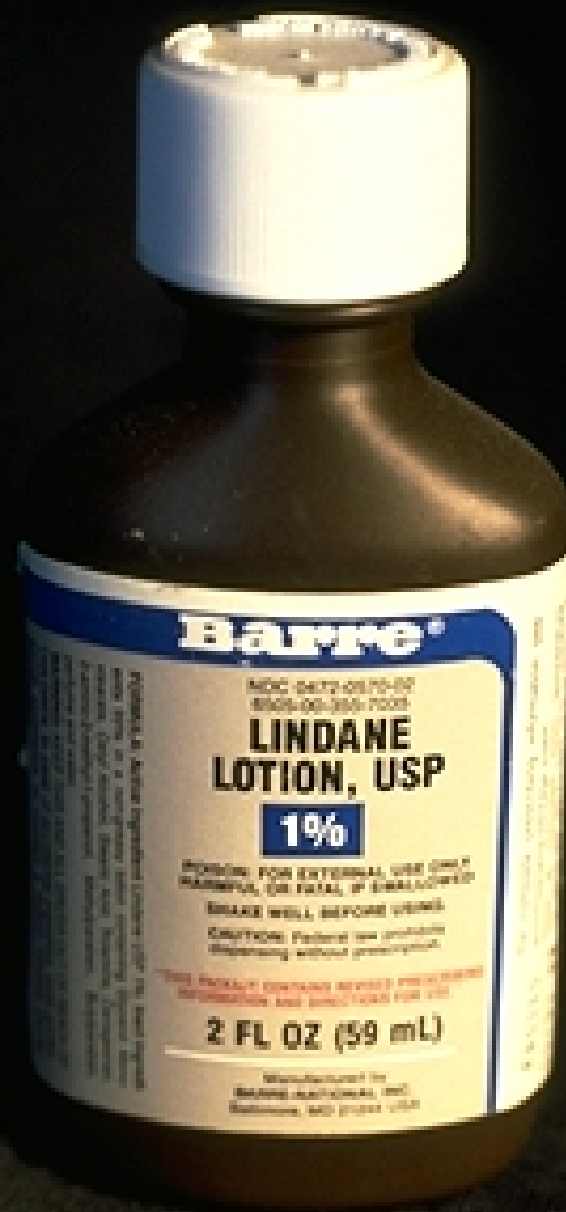
- **Blocks enzymatic synthesis of RNA and DNA**
- **Quinidine-like effects on the heart**
 - **Impaired conduction & contractility**
- **Half-life = 1-60 days**
- **In children, doses 2-3 x greater than therapeutic (< 1 gm) have been fatal within 2-3 hrs**

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^+



Barre®

NDC 0472-0870-02
NDC 001-355-7000

**LINDANE
LOTION, USP**

1%

POISON. FOR EXTERNAL USE ONLY.
HARMFUL, OR FATAL, IF SWALLOWED.

SHAKE WELL BEFORE USING.

CAUTION: Federal law prohibits
dispensing without prescription.

*THIS PRODUCT CONTAINS A RECALL PRESCRIPTION
INFORMATION AND INSTRUCTIONS FOR USE

2 FL OZ (59 mL)

Manufactured by
Barre Pharmaceuticals, Inc.
Baltimore, MD 21204 USA

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

Liquid

MAXIMUM STRENGTH

MAXIMUM STRENGTH
Anbesol
Anesthetic/Benzocaine 20%

Oral Anesthetic/Benzocaine 20%

- **Toothache**
- **Gum Pain**
- **Canker Sores**
- **Denture Pain**

NET WT .41 FL OZ (12 mL)

Do Not Use if plastic blister or backing material is broken or if backing material is separated from the plastic.



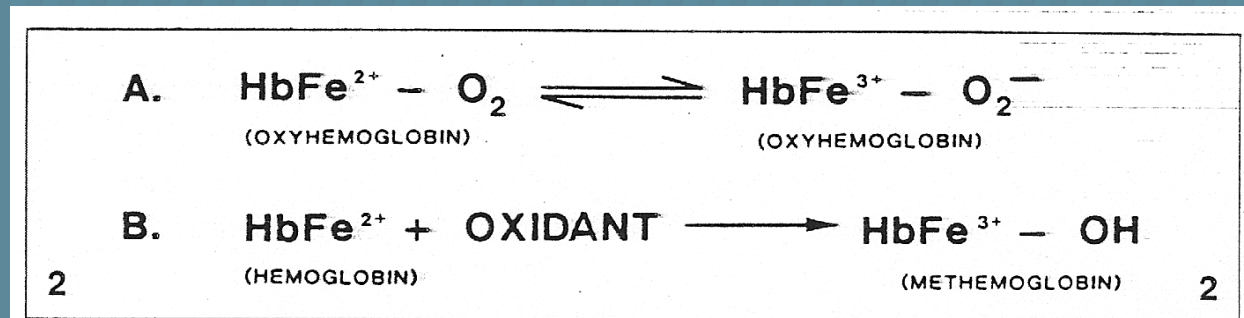
The left-hand package is the **Active Support Lite** for personal computers. It provides the **Warning Log** along with the other "core" features that the users should know about immediately after installation. It also contains a **Director's Edition**, which is a full supervisor for the product for up to 250 users. (See 42-037.)

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

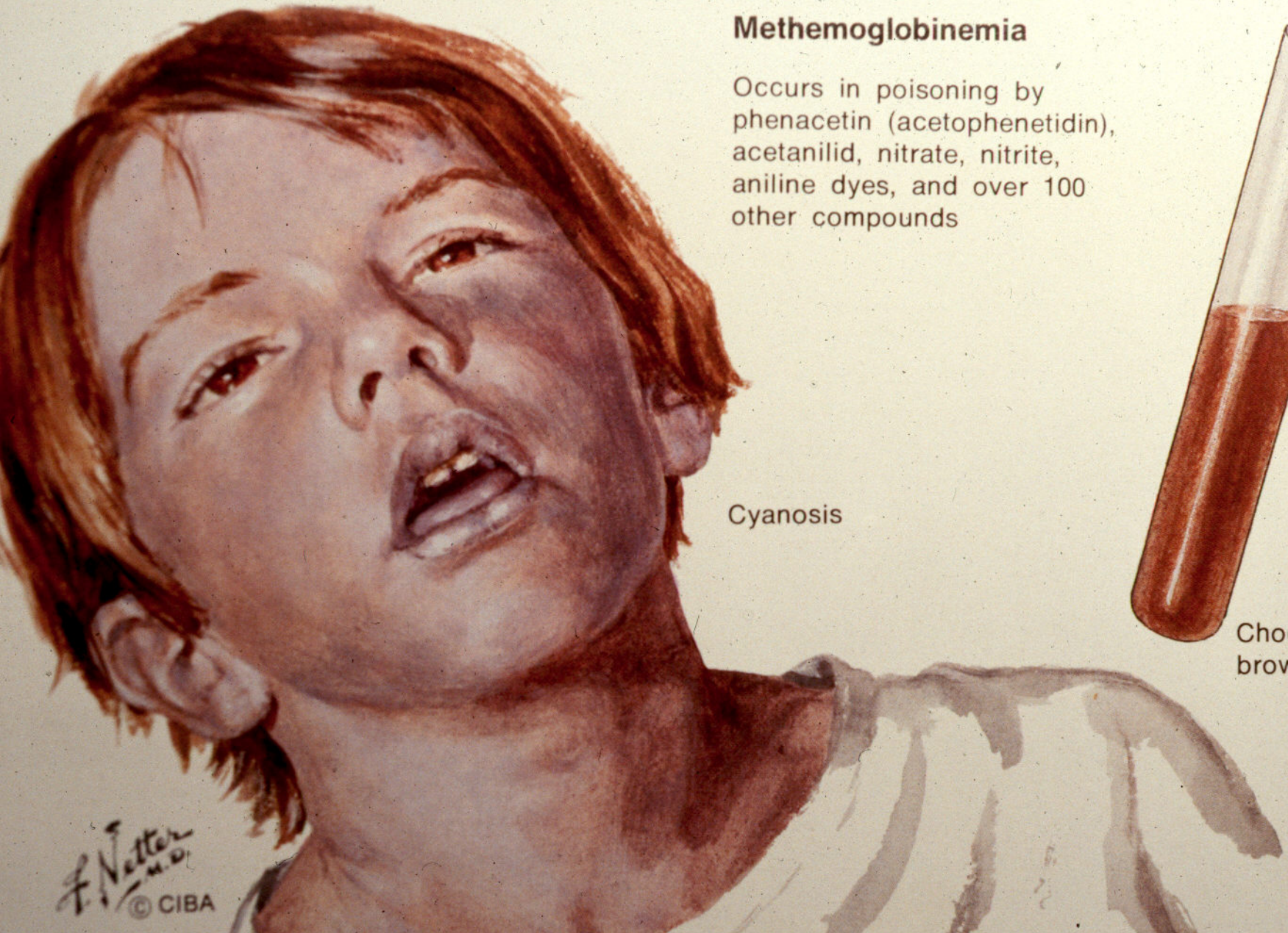
Methemoglobinemia

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

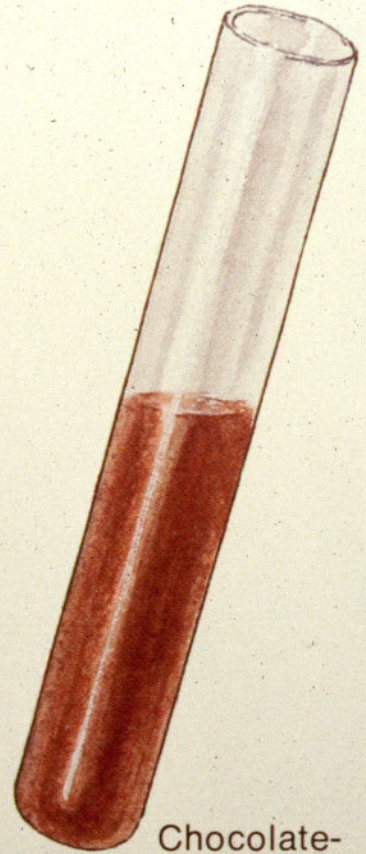


Methemoglobinemia

Occurs in poisoning by phenacetin (acetophenetidin), acetanilid, nitrate, nitrite, aniline dyes, and over 100 other compounds

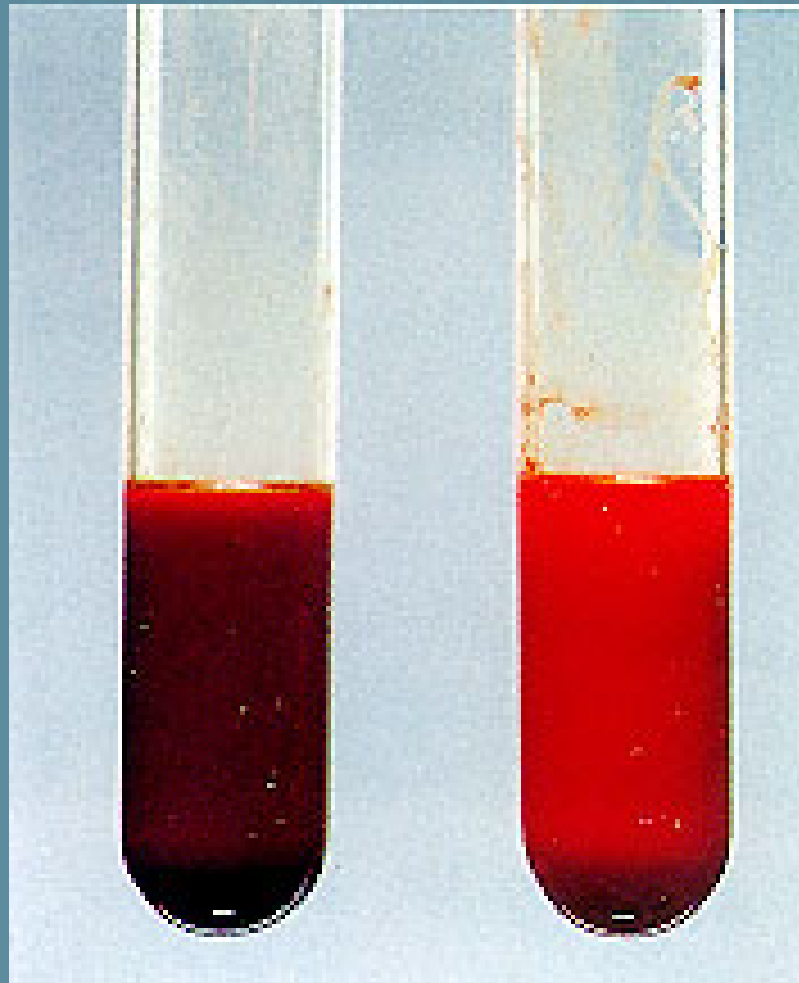


Cyanosis



Chocolate-brown blood

Methemoglobinemia



Methemoglobinemia



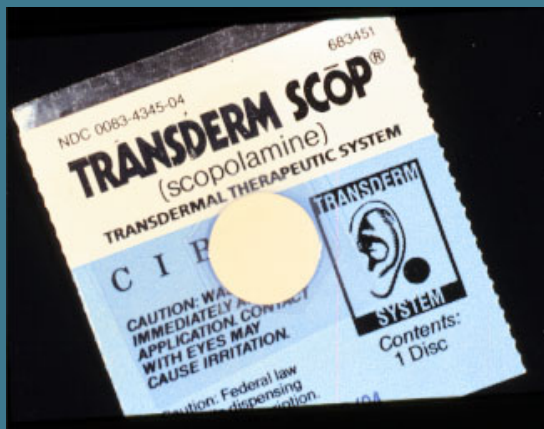
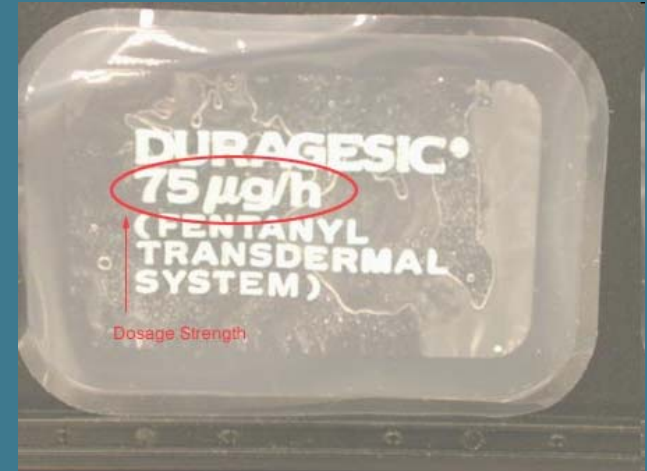
- Management = reduction of metHgb with methylene blue
- 1-2 mg/kg (0.1-0.2 ml/kg) of 1%
- May repeat at 1 hr intervals
- Avoid doses > 7 mg/kg

Discarded Transdermal Patches



Fentanyl

Catapres



Scopolamine

Nicoderm



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

Excitatory	Euphoria, excitement, dizziness, sneezing, coughing, drooling, N&V, bizarre behavior, hallucinations
Early CNS Depression	Confusion, disorientation, blurred vision, headache, pale, “buzzing”
Medium CNS Depression	Drowsiness, incoordination, slurred speech, random eye movements
Late CNS Depression	Coma, bizarre dreams, seizures

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

No, you can't leave yet.....

All of the following contain methylsalicylate except

- a. Oil of wintergreen
- b. Ben Gay ointment
- c. Icy Hot ointment
- d. Campho-phenique

Answer: d

Imidazolines are similar to what antihypertensive agent

- a. Beta blockers
- b. Clonidine
- c. Calcium channel blockers
- d. Ace inhibitors

Answer: b

Toxicity of camphor is primarily:

- a. Hepatic injury
- b. Metabolic acidosis
- c. Seizures
- d. Cardiac arrhythmias

Answer: c

Benzocaine exposure may result in:

- a. Coma
- b. Urinary retention
- c. Hypotension
- d. Methemoglobinemia

Answer: d

What toxidrome may be seen with Lomotil ingestion?

- a. Sympathomimetic
- b. Anticholinergic
- c. Cholinergic
- d. Opioid

Answer: b & d

Summary

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

