Pediatric Pharmacy Advocacy Group

Household Hazards

Jessica Hoover, Pharm.D., BCPPS
Erin Waehner, Pharm.D., BCPPS
Cleveland Clinic Children's
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Objectives

- Identify common household hazards that could result in life-threatening ingestion
- Illustrate pharmacists role in treating toxic ingestion
- Assess pharmaceutical treatment strategies of toxic household ingestion

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Poison Control Center Data

- 55 poison control centers (PCC) in the United States
- Someone called a PCC every 13 seconds in 2017
- 2.12 million human poison exposures in 2017
- 93% of exposures occur in the household

Poison Control Center Data Snapshot 2017. Available from https://piper.filecamp.com/1/piper/binary/3pnl-1u3j9614.pdf

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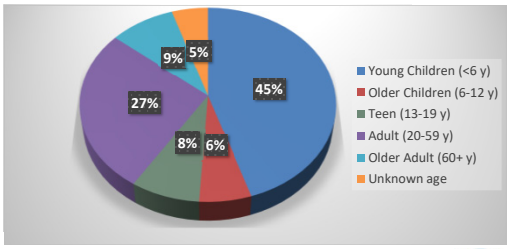
Age Distribution of Human Exposure Cases



Poison Control Center Data Snapshot 2017. Available from https://piper.filecamp.com/1/piper/binary/3pni-1u3j0614.pdf

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Top Substance Categories by Age Group

	Young Child (<6 y)	Older Children (6-12y)	Teen (13-19y)
Analgesics	9.2%	7.4%	21.3%
Antidepressants	<1%	<1%	12.3%
Antihistamines	4.7%	6.6%	6.9%
Cosmetics, Personal Care Products	12.6%	6.5%	2.7%
Foreign Bodies	6.4%	6.9%	<1%
Household Cleaning Substances	11%	4.9%	3.7%
Stimulants and Street Drugs	<1%	4.5%	5.3%
Topical Preparations	4.8%	<1%	<1%

Poison Control Center Data Snapshot 2017. Available from https://piper.filecamp.com/1/piper/binary/3pni-1u3j0614.pdf

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Epidemiology of Toxic Ingestions

- Most ingestions are associated with minimal toxicity
- Several products have the potential to cause severe toxicity and even death
- Toxic ingestions lead to 300,000 hospital admissions per year and 30,000 pediatric deaths per year

Bergen G, et al. 2007 Chartbook, National Center for Health Statistics

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Patient Case 1

- PM is a 6 month old male who presents to the ED after becoming floppy and unresponsive after a bottle feed
- Vitals: Temp: 97°F, BP: 89/50 mm Hg, Pulse: 120 bpm
- PE:
  - Fruity breath
- Initial lab values:

136	103	12	
4.0	25	0.35	42

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What agent is causing toxicity?

A. Ethanol
B. Methanol
C. Morphine
D. Lorazepam

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Sources of Ethanol

- Alcohol in unmarked bottles
- Alcoholic beverages
- Medications and Cosmetics
- Hygiene products
- Cleaning products




Royer P and Ratnapalan. Clin Peds 2012

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Clinical Manifestations of Ethanol Toxicity

Mild:
- Mucous membrane irritation
- Vomiting
- Tachycardia

Moderate-Severe:
- Hypoglycemia
- Metabolic acidosis
- Hypothermia
- Hypo-responsive
- Generalized tonic-clonic seizures

Royer P Clin Peds 2012
Edmunds SM et al. Pediatr Emer Care. 2014

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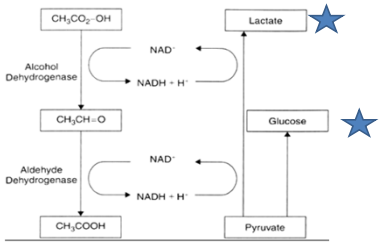
Mechanism of Ethanol Toxicity



Available from: usmle.biochemistryformedics.com/alcohol-induced-hypoglycemia

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Ethanol Toxicokinetics

Absorption: Rapid with a peak within 60 minutes
- Can be delayed by full stomach

Metabolism: via hepatic enzymes
- Patients less than 5 years old have immature dehydrogenase activity

Elimination: follows zero order kinetics
- Adults clear 20 mg/dL/hr
- Children may clear faster

Borought et al. Emergency Med. 2015
Edmunds SM et al. Pediatr Emer Care. 2014

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Ethanol Toxic Levels

- Ethanol levels ≥50mg/dL require emergent attention
- Levels ≥250 mg/dL are often associated with severe hypotension, coma, and hypoglycemia
- Lethal Dose 50 (LD_{50}):
  - 3 g/kg in children
  - 5 g/kg in adults

Borought et al. Emergency Med. 2015
Edmunds SM et al. Pediatr Emer Care. 2014
Royer P and Ratnapalan. Clin Peds 2012

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Treatment of Ethanol Toxicity

- Decontamination
  - Can consider gastric lavage
  - Activated charcoal does not bind to ethanol
- Supportive care:
  - Hypoglycemia → glucose
  - Metabolic acidosis → consider bicarbonate or intubation
  - Seizures → benzodiazepines
- Other treatment options:
  - Thiamine

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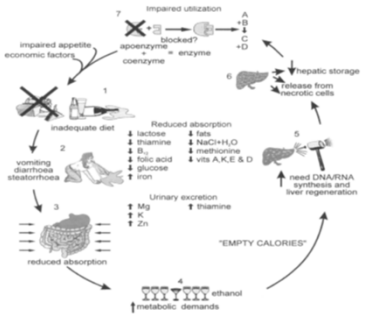
Thiamine Therapy in Pediatrics



Thomson AD. Alcohol and Alcoholism. 2000.

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Patient Case 2

- KR is a 15 month old female who presents to the PCP office with irritability, weight loss and vomiting
- Mom informs the physician that no one else in the house is sick but that they recently moved into a new house originally built in 1940 and they are “fixing it up”. Patient recently began walking and tends to put things in her mouth

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What agent could be causing toxicity?

A. Carbon Monoxide
B. Lead
C. Fertilizer
D. Bleach

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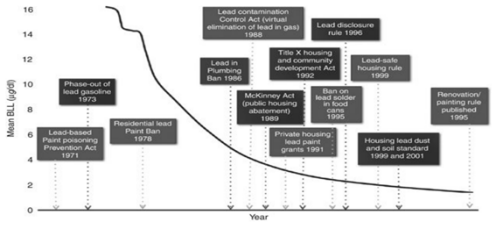
Decline in Childhood Blood Lead Levels (BLL)



Pediatric Research 83, 23-30 (2018)

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Risk Factors for Lead Poisoning

- Children younger than six years of age and particularly those younger than 36 months
  - Higher exposure to dust because of crawling
  - Higher respiratory rates
  - Hand-to-mouth behavior
- Deteriorating housing built before 1970
- Industrialized use

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Lead Toxicokinetics

- Absorption:
  - Dependent on route, age and nutritional status
- Metabolism:
  - Inorganic lead is not metabolized but is directly absorbed, distributed, and excreted
- Elimination:
  - Not retained in tissues
  - Excreted by the kidneys or through biliary clearance in the GI tract
- Children <2 years of age retain ½ of absorbed lead vs. adults retain only 1%

Available from cdc.gov/nceh/lead/ACCLPP/activities.htm

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Clinical Manifestations of Lead Poisoning

- Neurologic
  - Neurobehavioral deficits
  - Encephalopathy (BLL >100 mcg/dL)
- Renal
- Gastrointestinal
  - Lead colic
- Endocrine
- Hematologic

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Treatment of Lead Poisoning

Blood Lead Level	Treatment
<5 mcg/dL	-Repeat BLL in 3-12 months -Routine health maintenance assessments -Education on sources of lead exposure
5-14 mcg/dL	-Perform steps as described above for levels <5 mcg/dL -Repeat BLL in 1-3 months -Developmental screenings
15-44 mcg/dL	-Perform steps as described above for levels 5-14 mcg/dL -Repeat BLL in 1-4 weeks -Complete history and physical -Obtain hemoglobin, hematocrit and iron studies
45-69 mcg/dL	-Perform steps as described above for levels 15-44 mcg/dL -Complete neurologic examination -Chelation therapy
≥70 mcg/dL	-Perform steps as described above for levels 45-69 mcg/dL -Hospitalization with chelation therapy

Newman N, et al. Pediatrics. 2013

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Pharmacologic Agents for Chelation

Medication	Indication for Use	Dose	Monitoring
Succimer (Chemet®)	Asymptomatic children with BLL 45-69 mcg/dL	Oral: 10 mg/kg/dose Q8H x5 days then 10 mg/kg/dose Q12H x14 days	BLL Adverse effects: rash, neutropenia, increased LFTs, GI upset
Calcium disodium edetate	Single agent for asymptomatic patients with BLL 45-69 mcg/dL *Useful when can't tolerate succimer*	IM/IV: 1000 mg/m²/day x5 days	BLL Adverse effects: fever, hypocalcemia, renal dysfunction
Dimercaprol (Bal in Oil®)	Adjunct with calcium disodium edetate when BLL ≥70 mcg/dL	IM: 4 mg/kg every 4 hours x2-7 days	BLL Adverse effects: chest tightness, hypertension, tachycardia, fever
D-penicillamine (Cuprimine®)	3rd line agent for use when other agents not tolerated	Oral: 10-15 mg/kg/day x4-12 weeks	BLL Adverse effects: hematologic, SJS, increased LFTs

Pediatrics 2005;116:1036
Schroder A, et al. US Pharm. 2015;40(5): 40-44

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Patient Case 3

- BW a 2 year old male presents to the ED with possible ingestion. Patient has had strange muscle movements, copious secretions, and intermittent agitation.
- Vitals: BP: 93/70 mmHg, HR:150-155 that trended down into the 70s as he was observed
- Patient has received 0.1 mg/kg IV lorazepam and 0.15 mg/kg IV ondansetron with no resolution

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What is the most likely cause?

A. Marijuana
B. Nicotine
C. Laundry detergent
D. Toothpaste

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Sources of Nicotine

- Chewing Tobacco
- Cigarettes
- Cigars
- Nicotine patch
- Nicotine gum
- E. Cigarettes
- Plants

Noble MJ et al. Emergency Med 2017.
Normandin PA et al. Journal of Emerg Nurse. 2015

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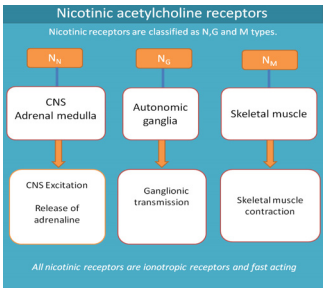
Mechanism of Toxicity



Noble MJ et al. Emergency Med 2017.
Normandin PA et al. Journal of Emerg Nurse. 2015
Available from: https://egpat.com/tutorials/cholinergic-agonists/nicotinic-receptors

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Nicotine Toxicokinetics

- Absorption: rapid and dependent on route
- Metabolism
  - Nicotine is metabolized into cotinine which is then mainly eliminated as 3'hydroxycotinine
- Half life ($T_{1/2}$)
  - Nicotine $T_{1/2}$= 40 minutes
  - Cotinine $T_{1/2}$= 16 hours
- LD_{50}
  - Not fully understood
  - Children 1-6 mg/kg/dose

Noble MJ et al. Emergency Med 2017.
Normandin PA et al. Journal of Emerg Nurse. 2015

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Treatment of Nicotine Toxicity

- Decontamination
  - Can consider gastric lavage
  - Activated charcoal does bind
- Supportive care
  - Seizures: benzodiazepines
  - Anti-cholinergic symptoms: atropine
- Possible options
  - Mecamylamine
  - Trimethaphan

Noble MJ et al. Emergency Med 2017.
Normandin PA et al. Journal of Emerg Nurse. 2015

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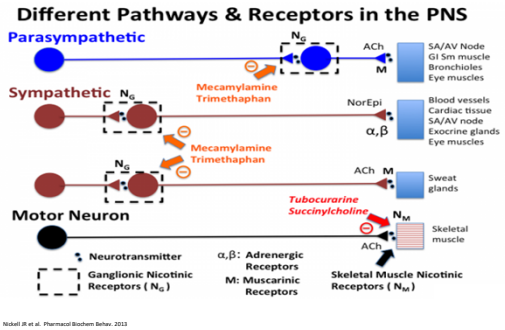
Nicotinic Antagonists



Nickell JR et al. Pharmacol Biochem Behav. 2013

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Patient Case 4

- WG is a 3 year old male who presents to the ED with nausea, vomiting and altered mental status
- Mother presents with similar symptoms and informs medical staff that symptoms began after eating items found during an afternoon walk 2 days ago
- Admission Labs:

AST	ALT	Alk Phos	Bili, Total	Albumin	Lactate	INR
13020	9282	354	1.7	4	1.7	7.4

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What agent could be causing toxicity?

A. Wild lettuce
B. Dandelion greens
C. Amanita mushroom
D. Wild blackberries

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Amanita phalloides Toxicity

http://www.mykoweb.com/CAP/photos/large/Amanita_phalloides%20mgw-25%29.jpg

- Death cap
- Contains toxins: amatoxins, phallotoxins, and virotoxins
- Variable concentrations and distribution of toxins
  - LD_{50}: 0.4-0.8 mg/kg
  - Lethal within 2-8 days

Vetter, J. Toxins of Amanita phalloides. *Toxicon*. 1998; 36(1): 13-24.

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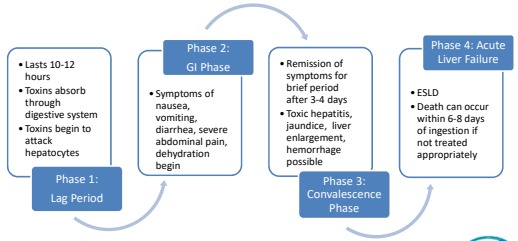
Mechanism of Amatoxin Toxicity



Vetter, J. Toxicon, 1998; 36(1): 13-24.
Broussard CN, et al. American journal of Gastroenterology, 2001. 96(11): 3195–3198

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Treatment for Amatoxin Ingestion

- Activated charcoal
- N-acetylcysteine (NAC)
- Amatoxin Inhibitors: Penicillin G and Silibinin
- Liver Transplant

Enjalbert F, et al. J Toxicol Clin Toxicol. 2002. 40(6): 715-757.

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Silibinin for Amatoxin Toxicity

Mechanism of Action	Amatoxin uptake inhibitor by OAT peptides and protects against the inhibition of RNA polymerase
Dosing Regimen	5 mg/kg infused over 1 hour, followed by continuous infusion of 20 mg/kg/day

- Most effective 24 hours post-ingestion
- Discontinue treatment if no sign of hepatic toxicity 4 days post-ingestion
- Clinical trial ongoing

Silibinin. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, OH. Available at [redacted]. Accessed November 13, 2018.

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Patient Case 5

- LG is a 5 year old presents to the ED with an ingestion of an unknown essential oil. Patient has been initially stable upon presentation.
- While being observed, patient became unresponsive and began having seizures.
- Lab values:
  - pH=7.18
  - ALT=650, AST=840, INR=5.3
  - Platelets= 32, Hb= 9.2

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Which essential oil was most likely consumed?

A. Wintergreen
B. Lavender
C. Clove
D. Fennel

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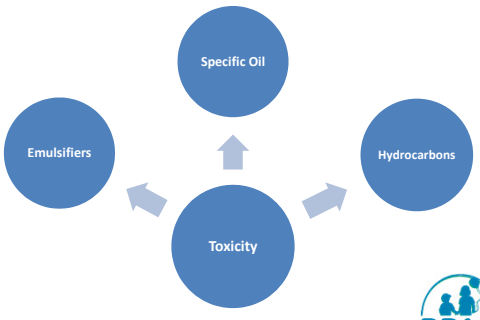
Mechanism of Essential Oil Toxicity



The Royal Children's Hospital, Melbourne, Australia, Clinical Practice Guideline on *Essential Oil Poisoning*

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Clinical Presentation of Essential Oil Toxicity

- Local irritation
- Gastrointestinal issues
- CNS depression
- Aspiration pneumonitis
- Oil specific toxicity

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Sources of Essential Oil Toxicity

Specific Oil	Clinical manifestations
Clove	Seizure, hepatotoxicity, renal failure, DIC
Fennel	Pulmonary edema, nausea, seizures
Geranium	Allergic contact chelitis
Lavender	CNS depression, ataxia, contact dermatitis
Thuja	Tonic-clonic seizures
Wintergreen	Salicylate toxicity
Wormwood	Acidosis, renal failure, rhabdomyolysis, delirium, paranoia, seizures
Eucalyptus	Rapid CNS depression

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Essential Oil Toxicokinetics

- Absorption:
  - Fat soluble substances
  - Well absorbed
- Metabolism
  - Dependent on oil
  - Typically through hepatic system or excreted unchanged
- Typically ingestion of >5 mL of essential oils can cause toxicity

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Clove metabolism

- Clove is known as eugenol which is metabolized in the liver
- Converts into a quinone intermediary which is thought to cause the direct damage to hepatocytes
- Eugenol causes depletion of glutathione similar to acetaminophen toxicity

Hartnoll G et al. Archives of Disease in Childhood. 1993
James SE et al. Eur J Pediatr. 2005

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Treatment of Essential Oil Toxicity

- Decontamination
  - Gastric lavage not recommended due to risk of aspiration pneumonitis
  - Activated charcoal binds to most oils
- Supportive care
  - Respiratory distress→ intubation
  - Rhabdomyolysis → fluid management
  - Seizures → benzodiazepine

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Clove Oil Treatment

- Hepatotoxicity:
  - N-acetylcysteine therapy should be utilized to replace glutathione stores
  - Use same dosing as acetaminophen toxicity
  - Multiple case reports show evidence of therapy success
- DIC
  - Combination of blood products, FFP and heparin

Hartnoll G et al. Archives of Disease in Childhood. 1993
James SE et al. Eur J Pediatr. 2005
Elwin JS et al. Journal of Toxicology. 2004

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How to Prevent Poisonings in Your Home

Available from: https://blog.mass.gov/blog/health/how-to-prevent-poisonings-in-your-home/

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QUESTIONS?

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