Pediatric Toxicology: Ingestions

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Question

- The majority of pediatric ingestions occur in which age group?
  - a. 6mo-1yr
  - b. 18mo-3yr
  - c. 4yr-6yr
  - d. 8-12 yr

Background

- Over 2.5 million reported human exposures to American Association of Poison Control Centers each year.
- 50% of these reported exposures in children <6yrs
- Unintentional ingestions <6yrs
- 30% of all intentional ingestions reported to AAPCC in children 6-19yrs
Background
- Most common pediatric exposures:
  - Cosmetics and personal care products
  - Cleaning agents
  - Analgesics
  - Cough/cold medications
  - Plants
  - Antihistamines
  - Pesticides

Question
- Which substance can kill a toddler in small amounts?
  a. Ibuprofen
  b. Methyl salicylate
  c. Bleach
  d. Ethanol
  e. Sertraline

Background
- Drugs and substances toxic in small amounts:
  - Benzocaine
  - B-Blockers
  - Calcium Channel Blockers
  - Camphor
  - Clonidine
  - Methyl Salicylate
  - Phenothiazines
  - Sulfonylureas
Background

• **FATAL “slp”**
  1. Camphor (Vicks VapoRub) 1000mg/5ml
     Fatal: 100mg/kg
  2. Methyl Salicylate (Wintergreen) 1000mg/1ml
     Fatal: 200mg/kg
  3. Benzocaine (Oragel)
     Toxic: 2ml, also causes metHgb, Sz

**Background**

• **“MALIGNANT swallow”**
  1. Chloroquine 20mg/kg
  2. Theophylline 8.4 mg/kg
  3. Chlorpromazine 25mg/kg
  4. Clonidine 0.3mg/kg: Bradycardia, CNS depression

History

• WHAT substance the child ingested: Often DIFFICULT
• WHEN?
• HOW MUCH?
• Names of ALL medications available to patient
• Symptoms and Treatment given prior to arrival
• Answers to these ?s—Severity of ingestion, need for therapeutic interventions, interpretation of drug levels, disposition of patient
Physical Exam

- Key Elements: HR, BP, RR, Temp, Pupils, Mental Status, Skin
- Toxidromes: Constellation of signs/symptoms that are suggestive of certain class of toxic substances:
  - Sympathomimetics
  - Anticholinergics
  - Cholinergic/Anticholinesterase
  - Opioids/Clonidine
  - Serotonin Syndrome
  - Sedative-Hypnotics

Case

- 2 year old brought to ED by EMS. Babysitter called EMS because she was difficult to arouse and found pills next to her. Babysitter doesn’t know what the pills are because the container not marked.
- Vitals: HR 50, BP 74/36, RR 5, temp 35.1
- PE: Will arouse to sternal rub, but falls back to sleep, miotic pupils

Case

- What did the child ingest?
  1. Acetaminophen
  2. Aspirin
  3. Benedryl
  4. Clonidine
  5. Pesticide
Case

- 13 year old brought to the ED by his parents because he "he isn’t acting right".
- Vitals: HR 120, BP 130/85, RR 18, Temp 37.8
- PE: Confused. Attempting to catch flies with his tongue. Dilated pupils, dry, flushed skin.

Case

- What did this teenager ingest?
  a. LSD
  b. Cocaine
  c. Jimson weed
  d. Ativan
  e. Tussinex

Case

- 15 year old female with hx of ADHD and depression presents brought to ED by EMS after mother found her on garage floor in a pool of vomit.
- VS: T34.9, RR 12, HR 122, BP 95/69
- PE: Extremely agitated when stimulated then obtunded, vomiting violently, pupils sluggishly reactive, Foley placed with return of green urine
Case

• What did this teenager ingest?
  1. Cocaine
  2. Coricidin D
  3. Pesticide
  4. I don’t know, Dr. Walsh. She makes absolutely no sense.

Toxidromes

• **Sympathomimetics**: ↑HR, ↑BP, ↑RR, ↑Temp,
  Agitation -> Seizures/Psychosis, Mydriasis, Diaphoresis
  Examples: Amphetamines, cocaine, pseudoephedrine,
  Caffeine, Albuterol

• **Anticholinergics**: ↑HR, ↑BP, ↑RR, ↑Temp, Altered
  MS, Delirium, Hallucinations, Mydriasis, Dry/flushed
  skin, Dry mucus memb, Urinary retention.
  Examples: Antihistamines, cyclic antidepressants,
  antispasmodics, jimsonweed, Atropine

• **Cholinergic/Anticholinesterase**: ↓HR, ↓RR, Temp
  and BP no change, Confusion->Coma, Miosis, Sweating,
  Diaphoresis, Bronchorrhea, Vomiting/Diarrhea
  Examples: Organophosphate pesticides, nerve
  agents/gasses, nicotine.

• **Opioids/Clonidine**: ↓HR, ↓BP, ↓RR/apnea, ↓Temp,
  Euphoria->lethargy->coma, Miosis
  Examples: Opiates, Clonidine, Imidazolines
  (tetrahydrozoline eyedrops)
Toxidromes

- **Serotonin Syndrome**: ↑HR, ↑BP, ↑Temp, Agitation ->Confusion->mania->coma, Mydriasis, Hyperreflexia, myoclonus, akathisia, seizures, rigidity
  - Examples: SSRIs, Dextromethorphan, meperidine, MDMA (ecstasy)

- **Sedative-Hypnotics**: ↓BP, ↓RR, ↓Temp, No HR change, Slurred speech, ataxia, depressed MS, mydriasis/normal pupil size, but sluggishly reactive
  - Examples: Benzos, Barbituates, Buspirone, Methaqualone

Management

- Always to basics: ABCs come first
- Check a glucose, treat with IV dextrose if hypoglycemia present
- Treat any hypotension initially with NS bolus
- Labs: BMP and VBG helpful. Drug levels for specific substances (Acetaminophen, aspirin).
- Urine drug screens not helpful in the acute management of the patient

Management

- GI Decontamination:
  1. Syrup of ipecac: No role
  2. Gastric lavage: Limited/minimal role
  3. Activated Charcoal: may have some effectiveness if used within 1st hour after ingestion, otherwise minimal benefit. May be role of multidose activated charcoal in some ingestions (theophylline, phenobarb).
Management

- Position State from American Academy of Toxicology, 2005
- Single-dose activated charcoal should not be administered routinely in the management of poisoned patients. Based on volunteer studies, the administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison (which is known to be adsorbed to charcoal) up to one hour previously. Although volunteer studies demonstrate that the reduction of drug absorption decreases to values of questionable clinical importance when charcoal is administered at times greater than one hour, the potential for benefit after one hour cannot be excluded. There is no evidence that the administration of activated charcoal improves clinical outcome. Unless a patient has an intact or protected airway, the administration of charcoal is contraindicated.

Management

- GI decontamination
  4. Whole Bowel Irrigation: May be used for ingestion of large amount of sustained released product or in body packers.
  Hemodialysis: Very specific uses, not common. E.g. severe aspirin toxicity, lithium, methanol, ethylene glycol

Management

- Antidotes:
  Naloxone: Opioids
  Flumazenil: Benzos. Do not use in chronic users -> seizures
  Fomepizole: Methanol and Ethylene glycol
  N-acetylcysteine: Acetaminophen
  Pralidoxime: Cholinesterase inhibitors
  Digibind: Digoxin
Specific Ingestions
- Acetaminophen
- Aspirin
- Beta-Blockers
- Calcium-Channel Blockers
- Clonidine
- Drugs of Abuse

Acetaminophen
- Common household
- High Use
- Easy Accessibility
- Intentional vs Unintentional Vs Chronic/Overmedicate
- Clinical presentation: Minimal signs/Sx
- Complication: Fulminant hepatic failure

Acetaminophen
- Metabolism: Primarily in liver thru glucuronidation and sulfation. Small percentage metabolized by cytochrome P-450 into toxic intermediate compound: NAPQI
- Recommended doses: NAPQI conjugated with glutathione->nontoxic metabolite->excreted in urine and bile
- Overdoses: Glutathione stores depleted->toxic build up of NAPQI->binds to hepatocytes->hepatocyte damage
Acetaminophen

- Main treatment issue: Prevention of hepatotoxicity
- Phases of overdose:
  1. <24 hours. GI Sx. Labs finding: Toxic Acet level
  2. 24-72 hrs. RUQ pain. Lab findings: Mild elevation LFTs
  3. 3-5 days. Jaundice, encephalopathy. Lab findings:
     Marked elevation of LFTs, coagulopathy, azotemia, hypoglycemia
  4. Approx 1 week. Gradual resolution of toxicity. Lab findings: Improvement in values.

Acetaminophen

- Predicting hepatotoxicity:
  1. By history elicited: acute ingestion of >7.5 gm in adult or >140mg/kg in a child generally predictive
  2. More accurate: Serum acetaminophen level obtained bw 4-24 hours after acute ingestion. Rumack-Matthew nomogram: plots serum concentration against hours post-ingestion, determines potential risk of hepatotoxicity
  3. Serial acetaminophen levels useful if accurate timing of ingestion cannot be obtained. Rising levels indicate potential hepatotoxicity

Acetaminophen

- Good news for kids: Toxicity often rare
- Theory is that acetaminophen metabolism in children shows a preference for alternative pathways other than the P-450 system.
- Conversion from juvenile to adult metabolism is thought to occur between 6-9 years of age.
Acetaminophen

- Acute ingestion within 24 hours
- Acute ingestion with unknown time or >24 hours
- Repeated supratherapeutic dosing

**TREATMENT:**

- **Activated Charcoal:** If within 1 hour of ingestion, possibly with SR preps
- **N-Acetylcysteine administration:** Binds directly to NAPQI, creating a nontoxic metabolite. Should be given as soon as possible after toxic level, up to 10 hours after ingestion. May be benefit even after that acute time frame.
- **Oral NAC (mucomyst):** Loading dose 140mg/kg, followed by maintenance dosing 70mg/kg every 4 hours for 17 doses
- **IV NC (Acetadote):** 150mg/kg over 15 min., followed by 50mg/kg over 4hr, then 100mg/kg over 16 hrs.

Higher rate of adverse rxns with IV use, esp anaphylaxis

Salicylate (Aspirin)

- Reduced poisonings in US due to increased use of aspirin alternatives, childhood proof containers, education on association with Reye syndrome in children
- Lack of awareness of aspirin-containing OTC meds: Pepto-Bismol, topical ointments/liniments (Oil of Wintergreen): Ingested or overuse of application
Salicylate

Clinical Presentation:
- Stimulate respiratory center of brainstem → early hyperventilation and respiratory alkalosis
- Interfere with glucose metabolism → hypoglycemia or hyperglycemia
- Uncouple oxidative phosphorylation → increased heat production, sweating, dehydration
- Gastric irritation → nausea/vomiting
- Stimulation of chemoreceptor zones → nausea/vomiting

Diagnosis:
- Serum level: acute vs chronic use, sustained release
- Serial levels: initial and 6 hrs should be obtained. In order to trend the severity of the poisoning
- Done nomogram: Limited, if any, value. Treatment should be based on serial levels and clinical status. The serum salicylate level does not itself reflect tissue distribution. If blood is acidemic, salicylate remains unionized, more penetrates the blood-brain barrier → increased CNS toxicity

Treatment
- If needs intubation: Need to maintain RR
- Hydration: 1.5-2x maint fluids
- Close glucose monitoring
- Alkalization blood and urine with NaHCO3: to increase the blood pH and trap the salicylate ion, limiting the amount crossing the blood-brain barrier.
- GI decontamination with multiple dose charcoal may be considered.
Beta-Blockers

- Used in both children and adults to control hypertension and arrhythmias, along with use for CHF, angina
- Mechanism: Block beta receptors - modulation of calcium-mediated excitation-contraction in smooth muscle
- Clinical effects: based on location of receptor
- Toxicity: Cardiac contractility and conduction delay
  - Sinus bradycardia common, not absolute
  - QRS prolongation and conduction abnormalities
  - Hypotension
  - Depressed MS and Seizures may occur

Beta-Blockers

- Overdose is common in children, but serious intoxication is rare
- Treatment: Increase the myocardial contractility by increasing the level of cAMP in cells.
  - Glucagon
  - Catecholamines: dopamine, epinephrine

Calcium Channel Blockers

- Most common agents: Verapamil, diltiazem, nifedipine
- Mechanism: Inhibit calcium flux thru low-voltage channels in cardiac and smooth muscle, as well as pacemaker cells in SA and AV nodes - vasodilation, myocardial depression, slowed nodal conduction
- S/Sx: Profound hypotension, bradycardia, resistant to treatment, cardiovascular collapse.
- Many sustained release preps on market: Symptoms may be early or even up to 16 hours after ingestion
**Calcium Channel Blockers**

- **Management**
  - Depends on amount ingested. Largely supportive
  - Correction of hypovolemia
  - Calcium gluconate: Creates concentration gradient large enough to partially overcome the channel blockade
  - Insulin and glucagon: High dose CCB inhibits insulin production and release → inability of heart muscle to utilize free fatty acids.
  - Inotropic support: dopamine, epinephrine
  - Cardiac pacing

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**Clonidine**

- Centrally acting antihypertensive agent
- Widespread use: hypertension, narcotic withdrawal, ADHD
- Mechanism: Stimulates central alpha receptors. No peripheral alpha receptor activity
- S/SX: Bradycardia, hypotension, CNS depression, miosis

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**Clonidine**

- Management for symptomatic patients
  - Surface warming for hypothermia
  - Fluid administration
  - Naloxone: single doses, often need a drip
  - Vasopressors
  - Atropine typically does not help the bradycardia.
Antidepressants

- 3 Broad categories:
  1. Tricyclic antidepressants (TCAs)
  2. Monoamine oxidase inhibitors (MAOIs)
  3. Serotonin uptake inhibitors (SSRIs)

SSRIs: Fewer side effects than TCAs and MAOIs, less toxicity, less adverse effects

Major side effects: Nausea, diarrhea, headache, agitation, panic attacks

Serotonin syndrome: Constellation of signs and sx: altered mental status, autonomic dysfunction, neuromuscular hyperactivity

TX: Supportive care and early recognition. Benzos may be used (help inhibit serotoninergic transmission), acetaminophen for fever, cyproheptadine may be used for sx d/t its nonspecific antagonism of serotonin receptors

Antidepressants

Tricyclic antidepressant (TCA) Overdose: An ED physician's nightmare

1. Patients may appear relatively well on initial exam and collapse rapidly
2. Need immediate care. Do not sit on a patient who has ingested large amounts of TCAs
3. TCA toxicity due to combo of: anticholinergic effects, quinidine-like effects (type 1a antiarrhythmic), alpha-adrenergic blockade, and antihistamine effects
Antidepressants

- TCA overdose symptoms: dizziness, confusion, blurred vision, dry mouth
- TCA overdose signs: Tachycardia, conduction blocks, QRS widening, hypotension, arrhythmias, cardiac arrest, delirium, agitation, myoclonus, seizures, urinary retention, hyper- or hypothermia

Antidepressants

- TCA overdose mgmt:
  1. Stabilize the ABCs, of course
  2. EKG essential!! Do on every patient presenting with possible TCA ingestion. Prolongation of ECG intervals should be considered a sign of TCA cardiotoxicity
  3. EKG changes: Due to the myocardial sodium channel blockade. Majority of patient at risk for seizures and arrhythmias will have QRS complex >0.10 seconds
  4. TX: Sodium bicarbonate: causes increased sodium conductance thru fast sodium channels and increased plasma protein binding of TCAs
  5. Treat hypotension with boluses and possibly vasopressors, DA or NE