Tennessee Poison Center: A Toxicology Overview

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Assistant Professor, Lipscomb University College of Pharmacy
Objectives

• Describe the purpose and role of the Tennessee Poison Center in the management of home and hospital exposures

• Compare and contrast the use of different gastrointestinal decontamination methods in toxic exposures

• Recommend appropriate treatment of the most common poison exposures including acetaminophen, aspirin, brown recluse spider bites, snake bites, and select drugs of abuse
National Poison Problem

- In 2014, approximately **2.9 million calls** were placed to local poison centers – AAPCC 2014 Annual Report
  - 2,165,142 human exposures
  - 56,265 animal exposures
  - 663,305 information calls
  - 6,085 human confirmed nonexposures
  - 112 animal confirmed nonexposures

- Poisonings were the **leading** cause of unintentional injury deaths in the US in 2012 - National Safety Council, 2014

- Poisonings were also the **leading** cause of unintentional injury death in Tennessee in 2016
State Poison Centers

• 24/7 resource for clinical toxicology consultation, poison prevention education, poison information
• Calls managed from both public and healthcare facilities
• Specialized services include
  • Language translation (150 languages)
  • TTY phones for the deaf
  • Toxicology Clinic
Poison Center Activities

- Phone consultations
- Surveillance
- Research
- Public education
- Professional Education
  - Learning site for pharmacy students and pediatric fellows
  - Chemical and Biologic Hazard Education
- TN Department of Health partner
- United Way
- webPOISONCONTROL partner
Types of Calls Handled by PCCs

- Pediatric ingestions
- Accidental Overdose
- Intentional Abuse
- Intentional Overdose
- Adverse Events
- Therapeutic Misuse
- Therapeutic Errors
- Environmental and Occupational

- Homeopathic products
- Plants
- Bites and Stings
- Chemical and Biologic Hazards
- Foodborne illness
- Toxicology laboratory questions
- Mercury or chemical spill clean-up
Tennessee Poison Control (TPC)

- A comprehensive poison resource center serving 6.5 million Tennessee residents
- Established in 1988
- Statewide program reaching all 95 counties
- Administratively associated with Vanderbilt University Medical Center
- **Mission**: To prevent poisonings, minimize poisoning complications and reduce the number of poison related deaths in Tennessee.
TPC Toxicology Experience

• Specialists in Poison Information (SPIs)
  • Pharmacists and nurses
  • Certification by national organization required

• Poison Information Providers (PIPs)
  • Uncertified specialists (pharmacists and nurses)
  • Pharmacy students

• Toxicology supervision
  • Medical director (MD) and managing director (Pharm.D.) board certified in clinical toxicology

• Public Health Education
  • Outreach to all 95 counties of Tennessee
Tennessee’s Poison Problem

- 50,849 total cases in 2016
  - 70% start at home
  - 30% start in a HCF
- 52% involved children < 6 years of age
- 59% involved pharmaceuticals
- 67% were managed on-site with telephone follow-up
- 2016: The TPC saved the state an estimated $8.8 million dollars in ED visits for the uninsured

1-800-222-1222
# Tennessee’s Poison Problem

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td>Analgesics</td>
<td>6,367</td>
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<tr>
<td><strong>2</strong></td>
<td>Household Cleaning Products</td>
<td>4,579</td>
</tr>
<tr>
<td><strong>3</strong></td>
<td>Cosmetics/Personal Care Products</td>
<td>4,301</td>
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<tr>
<td><strong>4</strong></td>
<td>Sedative/hypnotics/antipsychotics</td>
<td>3,169</td>
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<tr>
<td><strong>5</strong></td>
<td>Antihistamines</td>
<td>2,923</td>
</tr>
<tr>
<td><strong>6</strong></td>
<td>Cardiovascular drugs</td>
<td>2,704</td>
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<tr>
<td><strong>7</strong></td>
<td>Antidepressants</td>
<td>2,626</td>
</tr>
<tr>
<td><strong>8</strong></td>
<td>Foreign bodies/toys/miscellaneous</td>
<td>2,012</td>
</tr>
<tr>
<td><strong>9</strong></td>
<td>Pesticides</td>
<td>1,981</td>
</tr>
<tr>
<td><strong>10</strong></td>
<td>Topical preparations</td>
<td>1,696</td>
</tr>
</tbody>
</table>
TOP 10 COUNTIES FOR EXPOSURES

- Davidson: 24%
- Shelby: 20%
- Knox: 12%
- Hamilton: 10%
- Rutherford: 8%
- Montgomery: 6%
- Williamson: 6%
- Sullivan: 4%
- Sumner: 4%
- Washington: 4%
National Poisoning Data System

• Largest poison exposure database in the US
  • Exposure information from all 55 poison centers

• Poison center cases are uploaded to the National Poisoning Data System every 8 min – almost real time

• > 55 million poison exposures reported since 1983
  • Nationally, there are 6,230 exposures/day
  • With an average of 1 exposure every 13.8 seconds
Use of NPDS Data

- Surveillance of public health issues
- Trending of new and emerging threats
- Information on new product/medicine formulations
- Evidence to support actions/recalls of medications
- Education development
- Post-marketing drug surveillance
- Research
Toxidromes

- Anticholinergic
- Cholinergic
- Opioid
- Sedative / Hypnotic
- Sympathomimetic
- Serotonin Syndrome / NMS
Gastrointestinal Decontamination

- Activated Charcoal
- Whole Bowel Irrigation
- Gastric Lavage
- Ipecac

One does not simply Decontaminate the GI
Activated Charcoal

- **Mechanism of Action**: adsorption of chemicals into organic material

- **Indications**:
  - Single Dose: Ingestion of known life threatening drug with no antidote within an hour of ingestion
  - Multi-Dose: Carbamazepine, salicylates, phenobarbital, theophylline

- **Dose**: ideal toxic ratio 10:1
  - Adults: 25 to 50 grams
  - Pediatrics: 10 to 25 grams
Activated Charcoal

**Contraindications:**
- Drugs that cause CNS depression, seizures, altered mental status
- Drugs with an antidote
- Risk of aspiration
- Corrosive ingestions
- GI obstruction

**Utility:**
- Colchicine
- Rosary Peas (Abrin)
- Castor Beans (Ricin)
ACTIDOSE®
with SORBITOL

ACTIVATED CHARCOAL SUSPENSION

NDC 0574-0120-08

50 grams Activated Charcoal
96 grams Sorbitol

POISON ADSORBENT

Emergency Treatment for Accidental Poisoning

See attached package insert for dosage instructions and additional information.

If possible call a Poison Control Center, emergency medical facility, or health professional for help before using this product. If help cannot be reached quickly, follow directions under this label. Read label warnings and directions upon buying this product. Write emergency phone numbers in space provided.

Emergency Phone Number:

DIRECTIONS:
Shake Well. Unscrew color-coded cap and remove foil seal. Replace cap to administer.

TAMPER EVIDENT:
Do not use if imprinted protective seal under the cap is broken or missing.

NET CONTENTS: 240 mL (8 fl oz)

STORAGE: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]
Whole Bowel Irrigation

- **Mechanism of Action:** Polyethylene glycol in an electrolyte-based solution; “washout” of gastrointestinal tract

- **Indications:**
  - Visible iron tablets or Lithium
  - Drug packers
  - Extended-release drugs

- **Dose:**
  - Adults: 1 to 2 L per hour, continue until effluent is clear
  - Pediatrics: 500mL/h or 35 mL/kg/hr, continue until effluent is clear
Whole Bowel Irrigation

- **Contraindications:**
  - Ileus or obstruction
  - Drugs that cause CNS depression, seizures, altered mental status unless the airway is protected

"Wow, this prep is so delicious, I think I'll drink another!"
... said no one ever
Gastric Lavage

- **Mechanism of Action:** mechanical “washout” or “stomach pump”

- **Indications:** No evidence it improves clinical outcome and it may cause significant morbidity

- **Contraindications:**
  - Drugs that cause CNS depression, seizures, altered mental status unless the airway is protected
  - Corrosive substances
  - Children (due to tube size)
Ipecac

- **Mechanism of Action:** Emetic action by local mucosal irritation and action at the chemoreceptor trigger zone

- **Indications:** NO LONGER RECOMMENDED

- **Key Points:**
  - 30% of stomach contents returned at BEST
  - Need to administer very early post ingestion
  - Contraindicated in patients without a protected airway, ingestion of strong acids or alkaline agents, hydrocarbons, or agents with potential for quick onset of CNS depression or seizures
Poisoned Patients...
Patient Case #1

- 55yo M presents by EMS to the ED asymptomatic after reported ingestion of 15 Tylenol® Arthritis Strength about 2 hours ago in a self harm attempt.

- PMH: Diabetes, metformin, lisinopril
- Symptoms: nauseated, alert and oriented
- Vitals: HR: 80 BP: 133/98 RR: 18 T: 98.2

- What do you do first?
- 2 hour level: 162.7 mcg/mL
- 4 hour level: 115.2 mcg/mL
- 8 hour level: 98.2 mcg/mL
Acetaminophen (APAP)
APAP: Mechanism of Action / Toxicity

Acetaminophen (APAP, Paracetamol)

Liver

Urinary Excretion

Glucuronidation
Glucuronide and sulfate metabolites (non-toxic)

Sulfation
Cysteine conjugates and mercapturic acid (non-toxic)

APAP

2%

CYP

2E1

5~9%

NAPQI

Hepatocyte Necrosis

GSH-dependent path
APAP - Toxic Dose

- **Adult**
  - Acute: > 7.5 – 10g
  - Chronic: > 6g x2 or more days

- ** Pediatric**
  - Acute: > 200mg/kg
  - Chronic: > 150mg/kg x 2 or more days
Acetaminophen - PK

- **Absorption**
  - Varies based on formulation and is delayed by food and gut motility
  - Therapeutic serum levels: 10 - 20 mcg/ml

- **Distribution**
  - Protein Binding: 10 - 30%
  - Crosses placenta and blood / brain barrier
  - Vd: 0.7 - 2 L/kg

- **Metabolism**
  - 90%: hepatic conjugation to inactive metabolites
  - 5 - 15%: oxidized by CYP 2E1 to N-acetyl-p-benzoquinoneimine (NAPQI)

- **Elimination**
  - t 1/2: 2 - 3 hours
  - Metabolites excreted renally
# APAP – Clinical Timeline

<table>
<thead>
<tr>
<th>Stage</th>
<th>Time</th>
<th>LFTs</th>
<th>Labs</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1 to 24 hrs</td>
<td>No change</td>
<td>No change</td>
<td>N/V, diaphoresis, lethargy, malaise, asymptomatic</td>
</tr>
<tr>
<td>II</td>
<td>24 to 72 hrs</td>
<td>Increased</td>
<td>Increased PT, Scr</td>
<td>Right upper quadrant pain, N/V</td>
</tr>
<tr>
<td>III</td>
<td>72 to 96 hrs</td>
<td>Severely Increased</td>
<td>AKI, increased PT/INR, increased ammonia, lactic acidosis, hypoglycemia</td>
<td>N/V, diaphoresis, lethargy, malaise, jaundice, encephalopathy, cerebra edema, death</td>
</tr>
<tr>
<td>IV</td>
<td>96 hrs to 2 wks</td>
<td>Returned to normal</td>
<td>May take months to recover</td>
<td>Recovery, death, or liver transplant</td>
</tr>
</tbody>
</table>
APAP Labs

• Acetaminophen Serum Concentration
  • Draw > 4 hours after ingestion and repeat lab draw in 4 to 6 hours for ER form

• Aspartate aminotransferase (AST) – first lab to rise with liver injury
  • Ref range: 8 – 42 IU/L (adults) and 20 – 65 IU/L (peds)
  • AST > 1000 IU/L = hepatotoxicity
  • AST may elevate to the 10,000’s in severe APAP poisoning

• ALT, bilirubin, glucose

• PT/INR, pH, SCr
APAP - Treatment

• **N-acetylcysteine (NAC)**
  • MOA: Glutathione precursor, increasing glutathione stores, glutathione substitute, and enhances sulfation

• IV vs Oral (trade name differentiation)
  • Acetadote (IV)
  • Mucomyst (PO and inhalational)

• Indications
  • 4 hour level \( \geq 150 \text{mcg/mL} \)
  • Unknown time of ingestion with a level of \( \geq 30 \text{mcg/mL} \) OR AST / ALT elevation without medical cause

• Dose
  • 21 hour protocol IV
    • Bag 1: 150mg/kg in 200mL of D5W
    • Bag 2: 50mg/kg in 500mL of D5W
    • Bag 3: 100mg/kg in 1000mL of D5W
    • Bag 4: Repeat bag 3 dose, if APAP is still detectable or AST / ALT are elevated
Matthew-Rumack Nomogram
Patient Case #2

- 16yo F is transferred by EMS to the ED with severe tachypnea, tinnitus, and confusion after a reported ingestion of 120 enteric coated aspirin 325mg some time last night in a self harm attempt.

- PMH: previously healthy, no medications
- Symptoms: tinnitus, tachypnea, confusion, nausea, vomiting, febrile
- Vitals: HR: 110 BP: 115/68 RR: 38 T: 100.2

- What do you do first?
  - 18 hour level: 98 mg/dL
  - 24 hour level: 109 mg/dL
  - 26 hour level: 119mg/dL
Aspirin (ASA)
ASA – Mechanism of Action / Toxicity

**Mechanism of Action**

- Inhibit cyclooxygenase (COX) -> inhibiting production of prostaglandins (PGE). PGE mediate inflammation and fever
- Prevent platelet aggregation
- Directly inhibit neutrophils

**Mechanism of Toxicity**

- Central stimulation of the respiratory center → hyperventilation → respiratory alkalosis and compensatory metabolic acidosis (also contributes to dehydration)
- Intracellular effects – uncoupling of oxidative phosphorylation and interruption of glucose and fatty acid metabolism → contributes to metabolic acidosis
- Cerebral and pulmonary edema is due to an unknown MOT, may be due to alteration in capillary integrity
  - Decreased CSF glucose compared to plasma glucose
  - Hypoxia
  - ?
- Alters platelet function and may increase prothrombin time
ASA – Toxic Dose

- **Therapeutic Dose:** 10mg/kg
  - Therapeutic serum level 10 – 30 mg/dL

- **Toxic Dose**
  - **Acute**
    - **Pediatric:**
      - 150mg/kg – mild intoxication
      - 300mg/kg – severe toxicity
    - **Adult:**
      - 150mg/kg OR 6g
  - **Chronic** – 100mg/kg for 2 or more days

- **Toxic serum level:** >30 mg/dL potentially toxic
ASA – Pharmacokinetics

- **Absorption**: immediate, consider enteric coating, bezoars
  - At therapeutic concentrations (10mg/dL) = 90% protein bound
  - As serum levels rise the percentage bound to protein decreases
  - At 40mg/dL: 76% protein bound

- **Distribution**: Vd: 0.15 – 0.62 L/kg

- **Metabolism**: Rapidly hydrolyzed to salicylic acid then metabolized further

- **Elimination**: Primarily renal
ASA – Clinical Presentation

**Acute Toxicity**
- N/V
- Diaphoresis
- Tinnitus (subjective sensation of ringing, hissing or other sounds; may have hearing loss)
- Hyperventilation
- Mixed Acid-Base disturbances:
  - metabolic alkalosis early if excessive vomiting -> resp alkalosis (hyperventilation) -> compensatory metabolic acidosis + acidemia \(\rightarrow\) late, respiratory acidosis (grave prognosis)
- Deafness
- Altered Mental Status – agitation, hallucinations, drowsiness, coma
- Hyperthermia

**Chronic Toxicity**
- Hearing loss/tinnitus
- N/V
- Dyspnea/hyperventilation
- Tachycardia
- Fever
- Altered mental status – confusion, slurred speech, agitation, delirium

**slower onset and less severe appearance of symptoms may delay diagnosis**
**more common in elderly**
**common misdiagnosis: delirium, dementia, encephalopathy, FUO, Respiratory failure, cardiopulmonary disease (CHF, acute pulmonary edema)**
ASA - Treatment

- Serial salicylate levels: Q2 hrs until 2 levels < 30 mg/dL with last level at least 6 hours post ingestion

- Manage acid base disorders and electrolyte disturbances

- Allow permissive hypercapnea
  - Avoid intubation

- Consider enhanced elimination
  - Urinary alkalization: Sodium bicarbonate
  - Hemodialysis
Patient Case #4

• 28 yo M presents to the ED with previous painful bite a few nights before to the right upper arm below the shoulder. He presents with systemic rash, blanched / purple bruising to the arm, N/V, back pain

• PMH: previously healthy, no meds
• Symptoms: full body rash, blanched / purple bruising to the arm, N/V, brown urine, fever, myalgia
• Vitals: HR 85 BP 115/75 RR 14

• What do you do first?
Brown Recluse – Loxoceles reclusa

- Venom contains several cytotoxic enzymes
  - Sphingomyelinase D: dermatonecrotic enzyme = platelet aggregation and thrombosis of small capillaries
  - Hyaluronidase: facilitates local spread, causes erythrocyte hemolysis

- Presentation: mild bite, typically unremarkable
  - 24 hours: painful papule purple in color ➔ blanched with erythema ➔ ulceration / eschar
  - 24 to 72 hours: Fever, chills, N/V, myalgia, morbilliform rash, hemolysis
Brown Recluse – Loxoceles reclusa

• **Diagnosis:** R/O medical differential (cellulitis, MRSA, abscess)

• **Labs:** Urinalysis r/o hemolysis, CBC r/o hemolysis, DIC screen, renal function, type and screen PRN

• **Treatment:** No antibiotics, supportive wound care, blood prn, plastic surgery, no antivenom
Patient Case #5

- An 18 yo F comes into the ED after being bitten on the thumb by a snake while trail riding her bicycle. She stops to snap a selfie and when trying to pick it up, it bit her.

- PMH: previously healthy, no medications
- Symptoms: redness, swelling and tightness of the digit, pain and 2 visible fang marks on the thumb
- Vitals: HR: 110 BP: 125/71 RR: 15 T: 97

- What should you do now?
  - Swelling and tightness have progressed to the elbow, large purple blebs have started to form on her thumb
  - Platelets have dropped by half (425 to 215)
Rattle Snake - Crotalinae

- **Mechanism of toxicity:** Crotaline venom is very complex with many proteins / enzymes that cause cellular damage

- **Clinical presentation:** fang marks, edema, pain, ecchymosis, perioral numbness or tingling, diaphoresis, N/V, hypotension increased clotting time, decreased platelets, decreased H/H

- **Labs:** baseline coags, platelets, H/H, fibrinogen, d-dimer
  - Repeat all labs in 6 to 12 hours
  - Repeat all labs again in 2 weeks to check for delayed coagulopathies

- **Treatment:**
  - Wound Care – NO tourniquets, cutting or fasciotomies
  - Update tetanus
  - ELEVATE!
  - Antivenom if appropriate
    - Crofab: 4 to 6 vial bolus, then 2 vials every 6 hours for 3 doses
Patient Case #6

• 12yo M presents to the ED by private vehicle. His parents bring him in with a friend. The friend reports getting pills from another student at school. She says they took “skittles” – The patient is confused, agitated, and begins to seize while evaluating him.

• PMH: unknown
• Physical exam: Ocular nystagmus, mydriasis, normal mucus membranes, hyperreflexia, tonic - clonic seizures
• Vitals: HR: 160 BP: 90/54 RR: 14 T: 98.4 F

• What do you do first?
• Urine test: PCP +
Dextromethorphan
Dextromethorphan

• **MOA:**
  • Structurally related to opioids, NMDA antagonist with active metabolite dextrorphan

• **Clinical effects:**

<table>
<thead>
<tr>
<th>Plateau</th>
<th>Dose (mg/kg)</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5 to 2.5</td>
<td>N/V, euphoria, stimulation, intoxication, speech and motor movement difficulty</td>
</tr>
<tr>
<td>2</td>
<td>2.5 to 7.5</td>
<td>“Flanging”, hallucinations, nystagmus, double vision, tachycardia, double vision</td>
</tr>
<tr>
<td>3</td>
<td>7.5 to 15</td>
<td>Agitation, CNS depression, lethargy</td>
</tr>
<tr>
<td>4</td>
<td>&gt;15</td>
<td>Seizures, respiratory depression, pulmonary and cerebral edema,</td>
</tr>
</tbody>
</table>

**Toxic Dose:**
Adult and Pediatrics: >7.5mg/kg

https://erowid.org/chemicals/dxm/faq/dxm_experience.shtml
Dextromethorphan

- **Formulations**: tablets, liquid, gelcaps, lozenges, effervescent tablets

- **Labs**: salicylate, acetaminophen, EtOH, urine drug screen, CPK
  - Urine drug screen false +: PCP and methadone

- **Management**:
  - ABCs
  - Benzodiazepines
  - Symptomatic and supportive care

- **Antidotes**:
  - Naloxone: 0.4 to 2mg
Plateaus of dextromethorphan

Dosage Scale

http://dxm.darkridge.com/calc.html
http://dexcalt.com
Patient case #7

- 11yo M presents by EMS to the ED after being treated at an Urgent Care Clinic for anaphylaxis with epinephrine and steroids without symptom improvement.

- PMH: previously healthy, no medications
- Physical exam: severe swelling of the lips, otherwise mild overall discomfort

What do you do first?
Huffing

• **MOA:**
  - **Volatile hydrocarbons**: CNS depression due to GABA agonism, DA mediation, and NMDA antagonism, also K+ channel repolarization inhibition in myocytes
  - **Liquefied compressed gas**: adiabatic cooling = frostbite

• **Clinical effects:**
  - QTc prolongation, confusion, euphoria, syncope, hypoxia, fluorosis (rarely, chronically)

• **Labs**: EKG, CXR

• **Management:**
  - Airway support
  - Oxygen
  - AVOID anything that increases catecholamine release

Figure. The patient’s right elbow at presentation demonstrates a hypertrophic nodule.

Drugs in Pop Culture

http://www.92qnashville.com/2016/06/14/lil-wayne-and-his-addiction/
Drugs in Pop-Culture

• Purple drank, Sizzurp, Lean, Dirty Sprite:
  • Promethazine and codeine
  • Made popular by Three 6 Mafia, Lil’ Wayne, Hip-hop
    • Mixed with citrus soda and hard fruit flavored candy
  • Symptoms: Anticholinergic toxidrome, CNS and respiratory depression, seizures

https://s-media-cache-ak0.pinimg.com/564x/c2/42/dc/c242dc91afa549438b0c6be747bba284.jpg
Drugs in Pop Culture

• Molly, MDMA, Ecstasy
  • Hallucinogenic amphetamine
  • Symptoms: Confusion, euphoria, hyperthermia, hallucinations, seizures
Drugs in Pop Culture

• Gravel, Bath Salts, Flakka:
  • Synthetic cathinones
  • Symptoms: psychosis, anorexia, confusion, agitation, excited delirium, sympathomimetic toxi-drome
Summary

- The poison center is a free resource of professional medical advice with a toxicologist available 24/7.

- Gastrointestinal decontamination has limited utility. Always weigh risk vs benefit for EACH patient scenario.

- Be aware of the most common substances implicated in poisonings both intentional and accidental.

- Symptomatic and supportive care is the most important aspect of many poisoning scenarios.
Questions?
References
