The Science & Epidemiology of Adolescent Poisonings

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What Makes a Poison?

- The odor?
- The taste?
- The color?
- The substance?

Arsenic vs Water

Cyanide vs Oxygen

"The Dose Makes the Poison"

- Paracelsus

[Graph showing response vs dose with threshold]
How does one become poisoned?

• A - How’s it get in?
• D - Where does it go?
• M - What happens to it?
• E - How do you get rid of it?
Absorption

- Depends on route of exposure!
  - IV ~ instantaneous
  - INH/Sublingual/SQ ~ slightly slower
  - IM/Oral/Rectal ~ 15 min to 1 hour
  - Dermal ~ slowest & least efficient
Useful equations

- \[ t_{1/2} = \frac{0.693}{Ke} \]
  \[ Ke = \frac{0.693}{t_{1/2}} \]

- \[ CL = \frac{\text{Elim rate}}{C_p} \text{ or } Ke \times V_d \]

- \[ \Delta t = \frac{\ln C_1 - \ln C_2}{Ke} \]

\[ Cp = \left( \frac{Dose \times F}{V_d} \right) \times (e^{-Ke \times t} - e^{-Ka \times t}) \]
Absorption: Nature of Substance

- **Dosage Form**
  - Immediate vs Sustained Release
  - Depot Preparations

- **Pharmacologic issues**
  - Ex Anticholinergic
  - Fight vs Flight

- **Chemical properties**
  - Ionic
  - Weak acid/Weak base
Absorption

Solids are not absorbed!

Dissolution is usually the rate limiting step!
Absorption

- Passive Diffusion Through Pore
- Diffusion Across Membrane
- Carrier-Mediated Transport
Diffusion Across Membrane

Weak Acid

- (pH < pKa)

Weak Base

- (pH > pKa)

HA

A⁻

BH⁺
**Alteration of Urine pH**

**“Ion Trapping”**

**Tissues**

100x > [HA]

[H^+ + A^-]

**Blood**

100x > [HA]

HCO_3^- + K^+ → [HA]

[H^+ + A^-]

**Urine**

HCO_3^- + K^+ → [HA]

[H^+ + A^-]
Distribution

\[ \text{Cp} = D \times S \times F / V_d \]

Concentration = Amount (dose) / Volume

- 60 mg
- 6 L
- 10 mg/L
Distribution

Volume = Amount (dose) / Concentration

Gave 60mg
Concentration = 1 mg/L

\[ V = \frac{60\text{mg}}{1\text{mg/L}} \]
\[ V = 60 \text{ L} \]

Looks like your 60mg was dissolved into 60L instead of 6L due to unequal partitioning.

This is Apparent Vd!!
Protein Binding - Saturation

% Bound = Fraction of a therapeutic dose bound
Protein Binding - Interactions

A competing drug ↑ free fraction
Metabolism

- **Where does it occur?**
  - 1° Hepatic, 2° Renal
  - All Tissues have some metabolic capability

- **What is the purpose of metabolism?**
  - To increase water solubility of xenobiotics
  - Utilization of nutrients
Metabolic Reactions

- **Phase I: Asynthetic**
  - Oxidation: P-450
  - Hydroxylation
  - Reduction

- **Phase II: Synthethic**
  - Glucuronidation
  - Sulfation
  - Acetylation
  - Glycine
  - Glutathione
Metabolism - Saturation

Metabolic Pathway

1st order

Zero order

Log Concentration vs. Time

Graphs showing 1st order and Zero order metabolic pathways.

- 1st order: Log concentration decreases linearly over time.
- Zero order: Log concentration decreases with a more gradual curve over time.

Graphs depict the progression of concentration over time for each order.
Michaelis-Menten Kinetics

- Zero Order: \( \frac{dC}{dt} = V_{\text{max}} \)
- First Order: \( \frac{dC}{dt} = \frac{V_{\text{max}}}{K_{\text{m}}} C \)

Graph showing the concentration over time for zero and first-order reactions.
Metabolism P-450 Enzymes

Figure 13-12. Electron flow pathway in the microsomal drug-oxidizing system. (From Alvares & Pratt 1990, with permission.)
Metabolism - Inhibition

- **Competative**
  - 2 substances compete for the same site on the enzyme

- **Noncompeative**
  - Inhibitor binds to a different site than where drug is metabolized.

- **Uncompeative**
  - inhibition not related to enzyme (ie. Altered distribution)
Metabolism: P-450 Enzymes & Substrates

- Clinically significant subtypes
  - CYP 1A2
  - CYP 2D6
  - CYP 2E1
  - CYP 3A4
Elimination

• Major routes are
  – 1° Renal
  – 2° Hepatic/Biliary

• Depends on:
  – Blood flow to end organ
  – Water/Lipid Solubility
  – Volume of Distribution
  – Size: Smaller than protein
  – Not bound to protein
Hepatic/Biliary Elimination
Who gets poisoned & why?
AAPCC Statistics for 2001

* 2,168,248 Human Exposures
* 70% no or minimal effects
* 86% Unintentional
* 22% managed in HCF
  - 56% were T&R
  - 20% have serious clinical effects
* 52.7% involved children under 6 years of age
* 14.4% involved children 6 to 19 years of age
# COMMON SUBSTANCES OF EXPOSURE - AAPCC

<table>
<thead>
<tr>
<th>&lt; 6 years</th>
<th>6 to 19 years</th>
<th>&gt; 19 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>cosmetics</td>
<td>bite/stings</td>
<td>bite/stings</td>
</tr>
<tr>
<td>cleaning products</td>
<td>cleaning products</td>
<td>cleaning products</td>
</tr>
<tr>
<td>plants</td>
<td>foreign bodies</td>
<td>food poisoning</td>
</tr>
<tr>
<td>foreign bodies</td>
<td>cosmetics</td>
<td>cosmetics</td>
</tr>
<tr>
<td>pesticides</td>
<td>plants</td>
<td>pesticides</td>
</tr>
<tr>
<td>analgesics</td>
<td>analgesics</td>
<td>analgesics</td>
</tr>
<tr>
<td>cold &amp; cough</td>
<td>cold &amp; cough</td>
<td>sedative-hypnotics</td>
</tr>
<tr>
<td>topicals</td>
<td>street drugs</td>
<td>antidepressants</td>
</tr>
<tr>
<td>antibiotics</td>
<td>antidepressants</td>
<td>cold &amp; cough</td>
</tr>
<tr>
<td>GI preparations</td>
<td>antibiotics</td>
<td>antibiotics</td>
</tr>
<tr>
<td>vitamins</td>
<td>antihistamines</td>
<td>antihistamines</td>
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</tbody>
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### Reasons for Adolescent Poisoning

<table>
<thead>
<tr>
<th>Reason</th>
<th>6-12Y</th>
<th>13-19Y</th>
<th>6-19Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unintentional</td>
<td>138,756</td>
<td>81,101</td>
<td>219,857</td>
</tr>
<tr>
<td>Intentional</td>
<td>8,148</td>
<td>72,731</td>
<td>80,879</td>
</tr>
<tr>
<td>Other</td>
<td>1,555</td>
<td>2,019</td>
<td>3,574</td>
</tr>
<tr>
<td>Adverse reaction</td>
<td>2,332</td>
<td>3,493</td>
<td>5,825</td>
</tr>
<tr>
<td>Unknown</td>
<td>430</td>
<td>1,161</td>
<td>1,591</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>151,221</strong></td>
<td><strong>160,505</strong></td>
<td><strong>311,726</strong></td>
</tr>
<tr>
<td>Outcome</td>
<td>6-12Y</td>
<td>13-19Y</td>
<td>6-19Y</td>
</tr>
<tr>
<td>---------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>No Effect</td>
<td>24,668</td>
<td>27,472</td>
<td>52,140</td>
</tr>
<tr>
<td>Minor</td>
<td>26,816</td>
<td>40,256</td>
<td>67,072</td>
</tr>
<tr>
<td>Moderate</td>
<td>3,947</td>
<td>16,383</td>
<td>20,330</td>
</tr>
<tr>
<td>Major</td>
<td>246</td>
<td>1,589</td>
<td>1,835</td>
</tr>
<tr>
<td>Death</td>
<td>6</td>
<td>66</td>
<td>72</td>
</tr>
<tr>
<td>Unrelated</td>
<td>4,107</td>
<td>4,531</td>
<td>8,638</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>59,790</td>
<td>90,297</td>
<td>150,087</td>
</tr>
</tbody>
</table>
BACKGROUND ON POISONING IN ADOLESCENTS

- **National Mortality Statistics**
  - Accidental injuries are the leading cause of death in 10-19 year olds.
  - Suicides are the fourth and third leading cause of death in 10-14 year olds and 15-19 year olds, respectively.
- **Available on the WEB (http://wonder.cdc.gov/)**
- **Reported by medical examiners & hospitals**
- **Identifies race, gender, ICD-9 codes for cause of death**
- **Reports raw numbers and rates per 100K population**
Adolescent Poisoning Deaths

- Between 1979 and 1992
- 7,226 POISONING DEATHS
  - 3,777 Suicides
  - 3,449 Accidental
- Male : Female Ratio 1.8 : 1

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number</th>
<th>Rate (per 100K population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14 years</td>
<td>694</td>
<td>0.28</td>
</tr>
<tr>
<td>15-19 years</td>
<td>6,532</td>
<td>2.45</td>
</tr>
</tbody>
</table>
MORTALITY RATES FOR ADOLESCENT POISONINGS BY YEAR

DEATHS PER 100,000

ACCIDENTAL
SUICIDES
UNINTENTIONAL POISONING DEATHS
1979-1992

DEATHS PER 100,000

- ALL
- MALE
- FEMALE
- WHITE
- BLACK
- OTHER

10-14 yr
15-19 yr
SUICIDAL POISONING DEATHS 1979-1992

DEATHS PER 100,000

- 10-14 yr
- 15-19 yr

ALL  MALE  FEMALE  WHITE  BLACK  OTHER
Substances Responsible For Accidental Deaths By Age Group

10-14 YEARS OLD
- Drugs: 51%
- Other Solids/Liquids: 28%
- Gases/Vapors: 21%

15-19 YEARS OLD
- Drugs: 44%
- Other Solids/Liquids: 15%
- Gases/Vapors: 41%
Substances Responsible For Suicides By Age Group

10-14 YEARS OLD
- Drugs: 85%
- Other solid/liquid: 2%
- Gases/vapors: 13%

15-19 YEARS OLD
- Drugs: 53%
- Other solid/liquid: 3%
- Gases/vapors: 44%
Observations

Poisoning death rates were higher in males than females.

In 10-14 year olds majority of suicides involve drugs while accidental deaths more likely to involve non-drugs and gases.

In 15-19 year olds gases are most frequent substance followed closely by drugs for both suicides and accidental poisoning.

Poisoning is a more common means of suicide in adolescent females than males.

In 15-19 year old blacks the suicide rate was ~2/3 lower than all other races.
## Accidental Poisoning Deaths from Alcohols and Freon

<table>
<thead>
<tr>
<th></th>
<th>Number of Accidental Deaths (% of age group)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10-14</td>
</tr>
<tr>
<td>Alcohols</td>
<td>9 (1.9 %)</td>
</tr>
<tr>
<td>Freon</td>
<td>17 (3.7 %)</td>
</tr>
</tbody>
</table>
Substance Abuse Issues

- Ethanol
- Inhalants
- Cocaine
- Heroin
- Amphetamines
- Psychedelics

Anglo
African
Hispanic
STUDENTS
Inhalants

Sniffing ... Huffing ... Bagging
### Monitoring the Future Study

- Inhalant Use by Students, 2000: Monitoring the Future Study

<table>
<thead>
<tr>
<th></th>
<th>8th</th>
<th>10th</th>
<th>12th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever Used</td>
<td>17.9%</td>
<td>16.6%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Used in Past Year</td>
<td>9.4%</td>
<td>7.3%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Used in Past Month</td>
<td>4.5%</td>
<td>2.6%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>
Recommended by Physicians, Pharmacists and ... Dr. Feelgood??
What are they after?

- Dextromethorphan
  - Setrotonergic activity can produce visual & auditory hallucinations

- Antihistamines
  - Antimuscarinic properties produce visual and tactile hallucinations

- Decongestants
  - Stimulant effects
Patterns of use

- Cheap
- Readily available
- Not illegal
- Poor mans ecstasy
- Not much fun
- “Gateway drug”
- Most tend to use only a few times
- Poison center reports seem to indicate sporadic nature
Patients in TCADA Treatment Programs During 2000

- Ethanol
- Cocaine
- Heroin
- Amphetamines
- Ecstasy = 46
- GHB = 4
Hallucinogenic Amphetamines

- Phenylalkylamine structure
- Ring modifications to cause serotonergic effects
- MDMA - Ecstasy
  - MDEA
  - MDA
  - MBDB
Summary

Adolescent poisoning is a significant cause of morbidity and mortality.

As children age poisoning exposures become less frequent but more serious in nature.

Poison prevention in adolescents requires different educational strategies than for younger children due to more complex underlying causes.
Suggested References