Medical Management of Pesticide Poisoning:
Why We Need Diagnostic Tools

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Who I Am

• General Pediatrician & Academician
• MPH from Univ Alabama at Birmingham
  – Focus area of Pediatric Environmental Health
  – Lead poisoning and GIS
  – Pesticide poisoning and exposure
  – Environmental contributors to asthma
• Actively see patients in teaching setting
Recognition and Management of Pesticide Poisoning

• Co-Editor of 5th Edition– 1999
  – Acute Care Manual
  – New Chapters, References
  – English and Spanish

• Wide Distribution in US and Latin America

• Available On-line

• Chapter revisions for the 6th edition is currently underway
Changes from 5th Edition

- Revisions of all chapters
- Pyrethroids as a stand alone chapter
- New content in acute poisoning
  - Neonicotinoids and N-Phenylpyrazole insecticides
  - Glyphosate
- Chronic Effects
  - Neurological/neurodevelopmental
  - Cancer
  - Endocrine
  - Dermal
Medical School and Residency Training

• In medical school, ~ 7 hours on environmental health (EH) related topics (over all 4 years)\(^1\)
• US pediatric residency spends an average of two hours on EH related material\(^2\)
  – Highly dependent on presence of faculty with expertise
• RRC requirement to include environmental influences on health
  – “effects on child health of common environmental toxins, such as lead, and also of potential agents used in bioterrorism”

What most Physicians Know about Diagnosis

- Rely on clinician’s ability to recognize pesticide by clues in the history and PE
- My experience with students/ residents
  - They often equate “Pesticide” with “Insecticide”
    - (and “Insecticides” with “Organophosphates”)
  - Most can recall generalities of OP poisoning
    - Not differences between kids and adults
    - A differential diagnosis of pesticides?!
  - Rat poison equates “look for bleeding”
    - No institutional memory of convulsants
Home Use of Pesticides

- Insecticides are applied as a spray or powder in 66% of homes
  - 19% once a month
  - 14% two times a month or more often
- 12% said their doctor discussed pesticides
- Information sources for parents?
  - Pediatricians—52%
What most Physicians Know about Diagnosis

- 160 Washington DC area physicians\(^1\)
  - 69% did not diagnose pesticide toxicity
  - 53% had ever considered the diagnosis
  - 64% felt poorly prepared to answer patients’ questions about pesticides
  - 40% needed more information on pesticides

- Need for clinically relevant CME
- Greater discomfort with chronic or subacute toxicity

What most Physicians Know about Diagnosis

- Survey of teachers of pediatric environmental health
- Asked about abilities to teach specific subjects
  - >80% confident teaching about lead, tobacco smoke, asthma
  - 72% for carbon monoxide
  - 64% for mercury and neurodevelopment
  - 40% said they felt confident in teaching about pesticides (3rd lowest)

What most Physicians Know about Diagnosis

• OP poisoning may be different in kids than adults
  – Seizures (22-25% in kids)\textsuperscript{1,2} (2-3% in adults)
  – Mental status changes (lethargy/coma: 54-96%)\textsuperscript{1,2}
  – 80% transferred with wrong diagnosis\textsuperscript{1}

• Lack of diagnostic tests for many pesticides
  – Cholinesterase testing
  – Next step after that?

• Pesticide levels/metabolites?

# Poison Control Center Data

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Total/ mod to severe morb/ death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrethroids</td>
<td>25,569/ 2388/ 1</td>
<td>52,767/ 2333/ 4</td>
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<tr>
<td>Organophosphates</td>
<td>40,090/ 1994/ 21</td>
<td>28,503/ 1700/ 23</td>
</tr>
<tr>
<td>Carbamates</td>
<td>12,051/ 523/ 1</td>
<td>11,249/ 502/ 3</td>
</tr>
<tr>
<td>Strychnine</td>
<td>563/ 72/ 5</td>
<td>401/ 50/ 4</td>
</tr>
<tr>
<td>Paraquat</td>
<td>453/ 56/ 4</td>
<td>232/ 35/ 8</td>
</tr>
</tbody>
</table>

Compiled from Annual Reports from Poison Control Center Data; reported every fall in *Am J Emer Med* (at least until recently, now in *Clinical Toxicology*)
2006 Report of Poison Control Centers’ National Poison Data System

<table>
<thead>
<tr>
<th>Pesticide</th>
<th>Average 2001-03</th>
<th>2006</th>
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<tbody>
<tr>
<td></td>
<td>Total/ mod-severe morb/ death</td>
<td></td>
</tr>
<tr>
<td>Pyrethroids</td>
<td>17,589/778/1</td>
<td>26,083/889/3</td>
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<tr>
<td>Organophosphates</td>
<td>9,501/567/8</td>
<td>5,411/242/3</td>
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<tr>
<td>Carbamates</td>
<td>3,750/167/1</td>
<td>3,175/119/2</td>
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<tr>
<td>Strychnine</td>
<td>134/17/1</td>
<td>104/6/0</td>
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<tr>
<td>Paraquat</td>
<td>77/12/3</td>
<td>61/8/1</td>
</tr>
<tr>
<td>Boric Acid</td>
<td></td>
<td>4216/11/0</td>
</tr>
</tbody>
</table>

Bronstein AC, Spyker DA, et al. *Clinical Toxicology* 2007;45(8):815-917
Biomarkers in NHANES

- Organophosphates
- Carbamate
- Pyrethroid Insecticides
- Organochlorine Insecticides
- DEET metabolite
- Chlorophenoxy herbicides (2,4 D, etc)
- Atrazine
- *ortho*-Phenylphenol
- *para*-Dichlorobenzene (2,5-Dichlorophenol)
  - Moth balls, room deodorizer

NHANES = National Health and Nutrition Examination Survey
## CDC Biomonitoring Data
### 6-11 years

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Methyl Parathion (50%)</td>
<td>&lt;LOD</td>
<td>.790 µg/L</td>
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<tr>
<td>Chlorpyrifos (All)</td>
<td>2.88 µg/L</td>
<td>2.67 µg/L</td>
</tr>
<tr>
<td>Chlorpyrifos (12-19 yr)</td>
<td>2.37 µg/L</td>
<td>2.71 µg/L</td>
</tr>
<tr>
<td><em>3-Phenoxybenzoic acid</em></td>
<td></td>
<td>.325 µg/L</td>
</tr>
<tr>
<td>Deltamethrin</td>
<td>&lt;LOD</td>
<td></td>
</tr>
<tr>
<td>Cyfluthrin</td>
<td>&lt;LOD</td>
<td></td>
</tr>
<tr>
<td>Cypermethrin</td>
<td>&lt;LOD</td>
<td></td>
</tr>
</tbody>
</table>

*Metabolite of cypermethrin, deltamethrin, and permethrin

[http://www.cdc.gov/exposurereport](http://www.cdc.gov/exposurereport)
Organophosphate Metabolites
(Found in children’s urine)

Chlorpyrifos
  - 3,5,6 Trichloropyridinol
  - Diethylphosphate
  - Diethylthiophosphate

Parathion
  - Paranitrophenol
  - Dimethylphosphate
  - Dimethylthiophosphate

Methyl parathion
  - Dimethylphosphate
  - Dimethylthiophosphate

Malathion
  - Dimethyldithiophosphate
Pyrethroid Metabolites
(Found in children’s urine)

- Cypermethrin
- Deltamethrin
- Permethrin
- 3-Phenoxybenzoic acid
Biomarkers pro/con

- Allows population based data
- Helpful for research
- Tracking exposure in populations and comparing to national average

- Exposure does not equate to disease
- Not immediately accessible
  - No help to the clinician trying to manage a case
  - Not considered diagnostic
Pesticides with Diagnostics
(Some only of limited availability)

- OPs and Carbamates
- Paraquat and Diquat
- Arsenic
- Hydrogen Cyanide
- Brodifacoum (and other warfarins)
- Al and Zn phosphide
- Thallium sulfate
- Cholinesterase level*
- Dithionite test (colorimetric)#
- 24 hour urine*
- Cyanide ion (CN⁻)
- Prothrombin Time (PT)
- Hyperphosphatemia (non sp)
- 24 hour urine, also serum*

*Though available, still sent out to reference lab
#Questionable availability
Pesticides without available tests:

Or: Limited to Gov’t or University Lab
(Partial Listing)

- Organochlorines
- Strychnine
- Pyrethroids/pyrethrins
- Chloropicrin
- Chlorophenoxy herbicides
- Carbon disulfide
- Hexachlorobenzene

- Tetramethylenedisulfotetramine (TETS)
- Scilliroside (aka red squill)
- Neonicotinoids
- N-phenylpyrazones (Fipronil)
Neonicotinoids

- Insecticide; Marketed in US early 1990s
- Act on nicotinic ACh receptors (nAChR)
- While selective for insect nAChRs, human toxicity has been reported
- Limited understanding of the physiology
  - Targets central nAChRs
  - Other responses may include reduction of compound by the P450 system
  - Metabolic byproduct enters brain in mice
Neonicotinoids

- Human data limited to 4 reports, -- 2 deaths of autopsy-confirmed imidacloprid poisoning
- Excess nicotinic stimulation
  - Disorientation, agitation, drowsiness, loss of consciousness, tachycardia
  - Rhabdomyolysis, V-tach/V-Fib in severe cases
- Diagnostics not available
- This group is nowhere on health care provider radar screen

Infectious Disease Example

- Sore throat, feels hot
- Headache, fatigue
- Red throat, 103.8° F
- Swollen lymph nodes
- Half of his class was out last week with “swine flu”
- Mom is panicked
How do I know what it is?

- **Differential Diagnosis**
  - Gp A strep, Influenza,
  - (including H1N1)
  - Adenovirus, Mono
  - “other virus”

- **Rapid Test!**
  - Available for Strep throat and Influenza
  - Monosspot for mononucleosis
Treat Strep Throat:
Happy Outcome
Clinical Medicine is not always that clear…

- 4 year old child is brought in because he "doesn’t look right"
- Child is not responsive to voice
- Shortly after arrival you notice some twitching of his face, and his eyes look to the side
- Within minutes, this progresses to his whole body shaking all over
- Seizure last for about 3-4 minutes, but within 15 minutes they start up again, last longer, harder to stop
Managing the Seizure

- An IV is placed (with difficulty) and he requires several doses of ativan and a second medication before they stop, but so does his breathing
- On exam, he is now sedated, on the ventilator
- Temp of 101.6 °F, crackles in his lungs
- What do we have at our disposal to figure out why he is seizing?
Medical History

- In this case, often not so helpful
- Previous hx of seizures? Family Hx?
- Typically, a sound from the bedroom or toddler found lying on the ground
- Often initially a negative hx of any exposure
  - True in pesticide exposures
  - True in other cases (cocaine, stimulants, PCP)
  - Medications, sometimes more forthcoming
- Febrile illness preceded seizure?
Evaluating A Patient with Seizures

- Head CT/Brain MRI— No trauma, no abscess, bleed, or tumor
- EEG— may be helpful, diagnostic, or normal
- Spinal fluid culture— No Meningitis (48°)
- Rapid tests W. Nile v. and Herpes neg. (12-48°)
- Blood sugar and serum NA & Ca normal
- Lead level— typically 1 week, but can be STAT)
- Urine drug screen (positive for benzodiazepines)
- Cholinesterase testing is Normal
Needs
A Preliminary List

• Greater support for effective clinical education, particularly front line personnel
• Rapidly available diagnostic testing
  – As part of the registration process with EPA
• Improved therapeutic options
  – We have atropine and pralidoxime
  – Supportive care…
Summary

• As a reminder, pesticides were among the least of all PEH related topics that faculty felt comfortable teaching about.

• Having a way of testing would likely increase physician’s ability to consider and diagnose:
  – Lead level, chelation therapy
  – Cotinine, anti-smoking aids
  – Asthma, skin allergy testing; multiple options

• Helps diagnose a case, but also allows provider to reassure a patient if negative.