

US EPA ARCHIVE DOCUMENT

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
 - <http://www.epa.gov/oppfead1/safety/healthcare/handbook/handbook.htm>
- 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 material²
 - 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”

Schenk M, et al. *Acad Med* 1996; 71:499-501

Roberts JR, Gitterman B. *Amb Peds* 2003;3:57-59

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 physicians¹
 - 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

Balbus JM, et al. J Agromedicine 2006;11:27-38.

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)^{1,2} (2-3% in adults)
 - Mental status changes (lethargy/ coma: 54-96%)^{1,2}
 - 80% transferred with wrong diagnosis¹
- Lack of diagnostic tests for many pesticides
 - Cholinesterase testing
 - Next step after that?
- Pesticide levels/ metabolites?

Poison Control Center Data

| Pesticide | 1997-1999 | 2001-2003 |
|-----------|----------------------------------|-----------|
| | Total/ mod to severe morb/ death | |

- | | | |
|--------------------|--------------------|------------------|
| • Pyrethroids | • 25,569/ 2388/ 1 | 52,767/ 2333/ 4 |
| • Organophosphates | • 40,090/ 1994/ 21 | 28,503/ 1700/ 23 |
| • Carbamates | • 12,051/ 523/ 1 | 11,249/ 502/ 3 |
| • Strychnine | • 563/ 72/ 5 | 401/ 50/ 4 |
| • Paraquat | • 453/ 56/ 4 | 232/ 35/ 8 |

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

| Pesticide | Average 2001-03 Total/ mod-severe morb/ death | 2006 |
|-------------------------|--|--------------|
| • Pyrethroids | 17,589/778/1 | 26,083/889/3 |
| • Organophos -phates | 9,501/567/8 | 5,411/242/3 |
| • Carbamates | 3,750/167/1 | 3,175/119/2 |
| • Strychnine | 134/17/1 | 104/6/0 |
| • Paraquat | 77/12/3 | 61/8/1 |
| • Boric Acid | | 4216/11/0 |

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

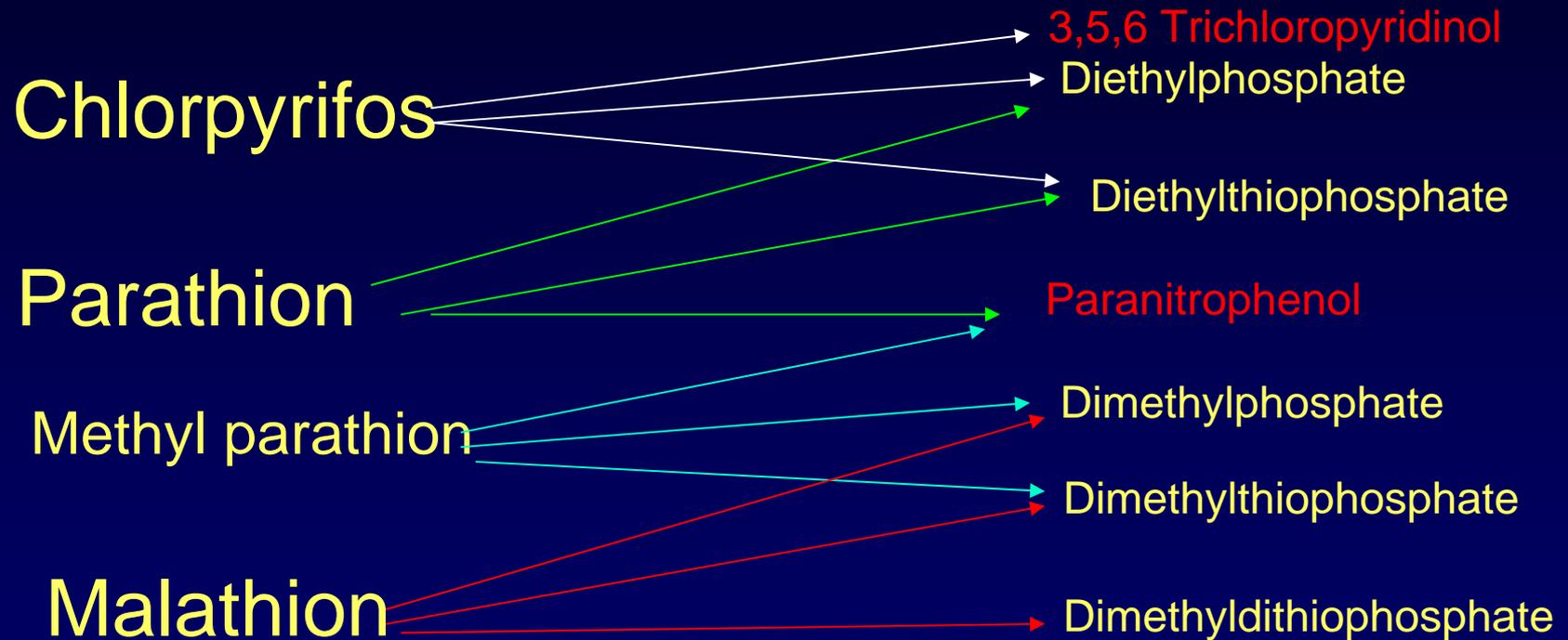
| Parent Compound | 1999-2000 | 2001-2002 |
|---------------------------|-----------|-----------|
| • Methyl Parathion (50%) | <LOD | .790 µg/L |
| • Chlorpyrifos (All) | 2.88 µg/L | 2.67 µg/L |
| • Chlorpyrifos (12-19 yr) | 2.37 µg/L | 2.71 µg/L |
| • *3-Phenoxybenzoic acid | | .325 µg/L |
| – Deltamethrin | | <LOD |
| – Cyfluthrin | | <LOD |
| – Cypermethrin | | <LOD |

*Metabolite of cypermethrin, deltamethrin, and permethrin

<http://www.cdc.gov/exposurereport>

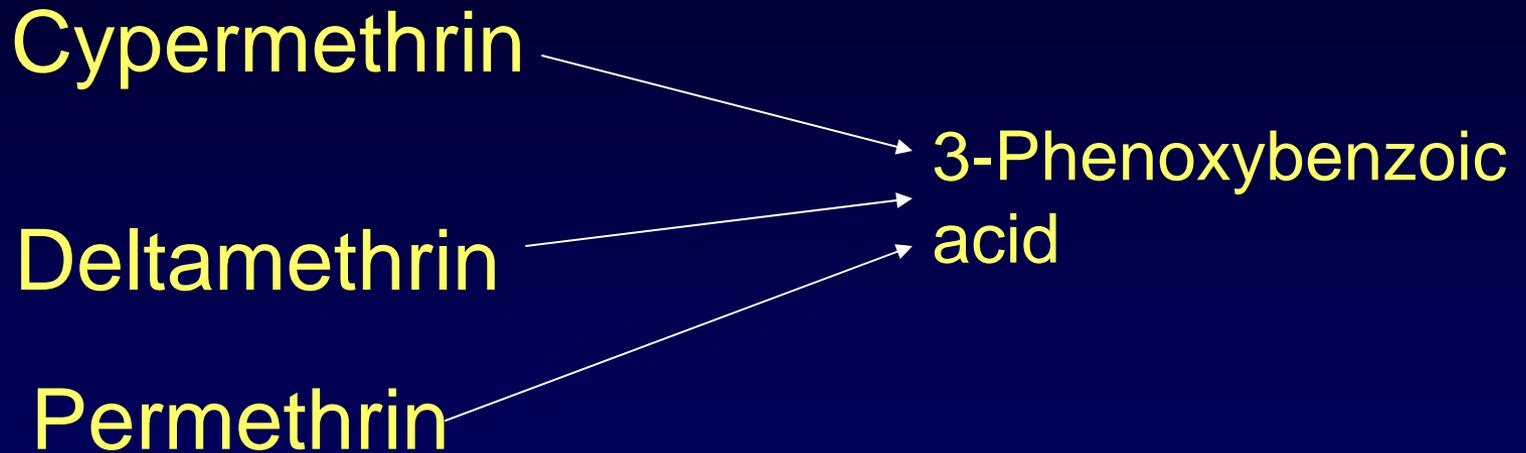
Organophosphate Metabolites

(Found in children's urine)



Pyrethroid Metabolites

(Found in children's urine)



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

Agarwal R, et al. Am J Emerg Med 2007;25:844-5
David D, et al, Clin Tox 2007;45:485-6
Huang NC, et al. Am J Emerg Med 2006;24:883-5
Wu IW, et al. J Tox clin Tox 2001;39:61 7-21.

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
 - Monospot 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