Disclosure and Disclaimer

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Disclosure: We have no real or perceived vested interests that relate to this presentation nor do we have any relationships with pharmaceutical companies, biomedical device manufacturers, and/or other corporations whose products or services are related to pertinent therapeutic areas.

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Learning Objectives

- Describe acute and chronic health effects of pesticide exposure
- Recognize multiple types and categories of pesticides
- Identify the clinical effects of active ingredients in commonly used pesticides
- Understand how to use the Recognition and Management of Pesticide Poisonings, 6th ed

Recognition and Management of Pesticide Poisonings, 6th Edition

Pesticide Exposure

- 10,000-20,000 occupational exposures per year in US (EPA 1996)
- Inconsistent and incomplete surveillance system
- Latinos farmworkers most exposed
- Over 1 billion pounds of pesticides used each year, mostly in agriculture

World-wide

3 million poisonings
200,000 deaths

Significant underreporting
~ 25 million poisonings (if all cases counted)

98% under-reporting to surveillance systems (Studies from Central America)
If You Remember One Thing...

- 80% of children with organophosphate poisoning were transferred with the wrong diagnosis.
- Acute pesticide poisoning may not be relatively common...
- But you need a high index of suspicion so that it is not missed.
4 month old child presents to ED

- Fussy, decreased appetite, vomiting, diarrhea, lethargic, limp
- Apnea reported, and en route “eyes roll back in head”
- ED exam: Limp, miosis, poor respiratory effort, increased amount of secretions
- HR 178, RR 34, T 98.6

What is your diagnosis?
4 Month old now in ICU

- Further hx: 5 previous hospital admissions, 1 of which OP suspected
- Sepsis workup negative
- Received fentanyl, pralidoxime, atropine
- RBC and plasma cholinesterase levels decreased
- Initial urine, blood, and breast milk samples negative for pesticides/metabolites
- Baby stabilized, remained in hospital during investigation of home, dad’s work

Organophosphate/Carbamate Acute Toxicity

- Phosphorylates acetylcholinesterase (AchE)
  - Excess Ach accumulates in nerve ending
- Classic findings: Hyper-secretion (muscarinic)
  - Salivation, lacrimation, bronchorrhea, perspiration, diarrhea, miosis
  - Less common in children than adults
- Skeletal muscle (nicotinic effects)
  - Excitatory (Muscle fasciculations)
  - Inhibitory (Weakness & paralysis) – this is actually a delayed finding in some cases of OP poisoning
Organophosphate Toxicity

• Central effects
  – Sensory/behavioral disturbance, incoordination
  – Respiratory depression, coma, seizures

• Autonomic ganglia
  – Classically see bradycardia--- sinus arrest
  – Tachycardia and hypertension from nicotinic receptors may precede bradycardia

• Cause of death
  – respiratory depression (central) exacerbated by excess pulmonary secretions

• Children v. Adults
  – Seizures in 8-39% of children v. 2-3% in adults
  – Lethargy and coma 55%-100% of pediatric cases

Treatment

• Recovery depends on generation of new enzyme
• Airway, oxygenation, and ventilation
• Atropine reverses some cholinergic effects
  – Frequent doses and higher doses are needed
  – Generally less effective against nicotinic or CNS actions
• Pralidoxime (organophosphate only)
  – Reactivates AchE
• Address possible exposures & report incident

Infant’s Home Environment

• Dad and uncle both farmworkers, living with their families in one farm trailer
• Both trained as pesticide handlers
  – Helped move pesticide containers but did not open or spray them
  – Wear same clothes home from field, but report washing them separately
• Moved to different trailer at discharge

4 Month at Home

• Tested wipe samples from original trailer
  – 2 different OPs
• Submitted new sample of infant’s urine to CDC for further testing
  – Acephate and dimethyl OP metabolites
• Set up decon room away from main living area
  – Still came home and ate lunch at table
  – Changed clothes, but no shower before holding baby
Understanding Pesticide Use
Survey of patients in 4 pediatric practices

• 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%
Physician/Medical Student Knowledge of Pesticides

• Clinician to recognize pesticide poisoning by clues in the history and PE

• My experience with students/ residents
  – They often equate “Pesticide” with “Insecticide”
  – Most can recall generalities of OP poisoning
    • Not differences between kids and adults
    • A differential diagnosis of pesticides?
  – “Rat poison” equates checking for bleeding
    • No institutional memory of convulsants (strychnine)
Which of the following is not an insecticide?

Commonly Presenting Signs and Symptoms

<table>
<thead>
<tr>
<th>Seizures</th>
<th>Nausea, vomiting, diarrhea</th>
<th>Respiratory distress, pulmonary edema</th>
<th>Headaches and Mental status changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>• drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• lethargy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• coma</td>
</tr>
</tbody>
</table>

| Skin findings     |                             |                                        | • rash                               |
|                   |                             |                                        | • blistering                         |
|                   |                             |                                        | • contact dermatitis                 |

| Cardiovascular    |                             |                                        | • tachycardia                        |
|                   |                             |                                        | • bradycardia                        |
|                   |                             |                                        | • hypotension                        |
Worker Exposure to Pesticides

- Mixing, Handling, Applying Pesticides
- Working in Fields/Orchards Treated with Pesticides
- Drift

Exposure to Family Members

- “Take home” exposure
- Drift
- Home application of pesticides
- Lawn and vegetable and flower gardens
25 year old with mental status changes

- A semi-comatose patient is brought in by EMS
- Patient initially complained of stinging, burning and numbness on hands, arms and face after working in the fields
  - Experienced headache, dizziness, nausea, vomiting
  - Mental status changes eventually occurred
  - Initially not clear what he was exposed to

- Increased oral secretions were noted
- Cyanosis and crackles present
- Muscle fasciculations were noted
- HR variable, tachycardic at times
  - Now bradycardic and occasional PVC’s
- Seizure activity within 30 minutes

Is it another case of OP poisoning?
What signs or symptoms pointed you away from Organophosphates?

Patient Management

• Appropriate decontamination takes place
  – Showered, clothes removed and bagged
  – Hospital employee protection
• Airway and breathing support
  – Seizures controlled with lorazepam
• Treatment with atropine and pralidoxime while awaiting cholinesterase levels
• Our patient is a little better, but still sick and appears different than at presentation
  – Now has flushed and hot, dry skin
  – Mydriasis, increasing tachycardia

• Otherwise responded to supportive care
  – Seizures stopped, more alert
  – Cholinesterase levels within normal limits

• Co-worker confirms use of cypermethrin
  – Type II (“Cyano”-pyrethroid)

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**Pyrethrins/Pyrethroids**

• Used worldwide since the 1970s
• Derived from the Chrysanthemum
• Pyrethrins—Short acting, unstable to heat/light, knockdown effect
  • Used for flying indoor pests, (wasp killer)
• Pyrethroids are synthetically modified
  • Outdoor control, agriculture, ectoparasites
  • Very common in consumer products
Chapter 4
Pyrethrins and Pyrethroids

Pyrethrins

Pyretherins are the oleoresin extract of dried chrysanthemum flowers. The extract contains about 50% active insecticidal ingredients known as pyrethrins. The lactone-esteric esters of chrysanthemic and pyrethric acids are known as pyrethrins, cineorins and jasmomins. These strongly lipophilic esters rapidly penetrate many insects and paralyze their nervous systems. Both crude pyrethrum extract and purified pyrethrins are contained in various commercial products, commonly dissolved in petroleum distillates. Some are packaged in pressurized containers (“bug bomb”), usually in combination with the synergist piperonyl butoxide and pyrethrin with dodecanol as a dispersant. The synergists related enzymatic degradation of pyrethrins. Pyrethrum and pyrethrin products are used mainly for indoor pest control. They are not sufficiently stable in light and heat to remain as active residues on crops. The synthetic insecticides known as pyrethroids (chemically similar to pyrethrins) have the stability needed for agricultural applications. Pyrethroids are discussed separately below.

Toxicology

Crude pyrethrum is a dermal and respiratory allergen, probably due mainly to non-insecticidal ingredients. Contact dermatitis and allergic respiratory reactions (rhinitis and asthma) have occurred following exposures. Single cases exhibiting anaphylactic and pneumonitis manifestations have also been reported. Pulmonary symptoms may be due to inhalation of the hydrocarbon vehicle(s) of the insecticides. The refined pyrethroids are probably less allergenic but appear to retain some irritant and/or sensitizing properties.

Pyrethrins are absorbed across the gastrointestinal tract and pulmonary membranes, but only slightly across intact skin. They are very effectively hydrolyzed to inert products by mammalian liver enzymes. This rapid degradation, combined with relatively poor bioavailability, probably accounts in large part for their relatively low mammalian toxicity. Dogs fed extraordinary doses exhibit tremor, ataxia, labored breathing and salivation. Similar neurotoxicity has been rarely observed in humans, even in individuals who had extensive contact from using pyrethrin for body lice control or have ingested pyrethrin as an anthelminth.

In cases of human exposure to commercial products, the possible role of other toxicants in the products should be kept in mind. The synergists piperonyl butoxide and dodecanol/silicone surfactants have been found, experimentally, to increase toxicity to humans, which...
CHAPTER 4
Pyrethrins & Pyrethroids

Pyrethrins

HIGHLIGHTS
Low systemic toxicity via inhalation and dermal route
Sites of action: sodium & chloride channels, GABA, nicotinic acetylcholine, peripheral benzodiazepine receptors
Type I (e.g., permethrin) usually do not contain a cyano group
Type II (e.g., cypermethrin, fenvalerate) always contain a cyano group
Type I acute poisonings are generally more severe

Signs & Symptoms
Type I: fine tremor, reflex hyperexcitability
Type II: severe salivation, hyperexcitability, chooroesthesia
May include dizziness, headache, fatigue, vomiting, diarrhea
Stinging, burning, itching, tingling, numb skin may be reported
Severe cases: pulmonary edema, seizures, coma

TREATMENT

Pyrethroids

HIGHLIGHTS
Low systemic toxicity via inhalation and dermal route
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TREATMENT

A report of illness in 27 farmers and 4 emergency responders was related to pyrethroid drift of the pyrethroid cyfluthrin. In this episode, the most commonly reported symptoms were headache (96%), nausea (89%), eye irritation (70%), muscle weakness (70%), anxiety (67%), and shortness of breath (64%).

Apart from central nervous system toxicity, some pyrethroids do cause distempering phenomena when liquid or volatile materials contact human skin. These symptoms
“Other Insecticides”
Neonicotinoids (Imidacloprid)

- Introduced in US market in 1990s
- Used in agriculture and for flea control
- Modified from nicotine
- Displaces ACh
  - Selective binding to insect Ach receptors
  - Consequently, less human toxicity
Neonicotinoid Toxicity

- **GI effects**
  - Vomiting, sore throat, abdominal pain\(^1\)
  - Ulceration throughout GI tract (solvent?)
- **Excessive nicotinic receptor stimulation**
  - Disorientation, agitation, weakness, LOC
- **Severe poisoning**
  - Rhabdomyolysis\(^2\)
  - Tachycardia, progressed to v-tach, v-fib\(^3\)


Fipronil

- Introduced to the US market in the 1990s
- Agriculture, lawn treatments, roach bait stations, household pet application
- Inhibits GABA gated Cl\(^-\) channels
  - Hyperexcitability of the cell
- High affinity for insects compared to mammals
  - 128x more toxic to insects than mammals
Fipronil

- Majority of cases with mild clinical effects and/or short duration
- Nausea/vomiting, dizziness, headache, abdominal pain
- Altered mental status, agitation, LOC
- Seizures
  - Usually self limiting

Lee SJ et al. Clin Toxicol 2010;48:737-744*
*Analysis of surveillance data from 2001-2007, 103 cases

Index of Signs and Symptoms
Starts on Page 244
<table>
<thead>
<tr>
<th>SYSTEM: Liver</th>
<th>SYMPTOMS/CAUSES</th>
<th>CHARACTERISTIC OF DISORDER</th>
<th>MAY OCCUR IN THESE POISONINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>Organophosphates, N-methyl carbamates, Paraxyl, Diquat, Nicotine, Metaldehyde, Fluoride, Borate, Phosphorous, Phosphides, Inorganic arsenicals, Sodium compounds, Copper compounds, Thallium, Organotin compounds, Neonicotinoids</td>
<td>Chlorophenox compounds, Aliphatic acids, Sodium chlorate, Creosote, Endothall, Aminopyridine, Coumarins, Indandiones, Fumigants (ingested)</td>
<td>Cytotoxins</td>
</tr>
<tr>
<td>Constipation</td>
<td>Pyrimidin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SYMPTOMS/CAUSES</th>
<th>CHARACTERISTIC OF DISORDER</th>
<th>MAY OCCUR IN THESE POISONINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enlargement</td>
<td>Copper compounds, Inorganic arsenicals, Sodium borate, Sodium fluoride, Sodium nitrite, Sodium nitrates, Sodium phosphides, Copper compounds, Thallium, Organotin compounds, Neonicotinoids</td>
<td>Chlorophenox compounds, Aliphatic acids, Sodium chlorate, Creosote, Endothall, Aminopyridine, Coumarins, Indandiones, Fumigants (ingested)</td>
</tr>
</tbody>
</table>

**Liver**

**Kidney**

*Jaundice (see section on Skin)*
Pesticides Known to Cause Seizures/Tremors

- **Insecticides**
  - Organochlorines, organophosphates, pyrethroids, nicotine, fipronil
- **Rodenticides**
  - Strychnine, sodium fluoroacetate, thallium, Al- and Zn phosphide
- **Herbicides**
  - Diquat, chlorophenoxy compounds (2,4-D)
- **Fumigants**
  - Cyanide, carbon disulfide, acrylonitrile, methyl bromide

Which pesticide is most commonly reported to the Poison Control Center?
### Pesticide Total Morbidity Death Total Mod- Severe Morbidity Death

<table>
<thead>
<tr>
<th>Pesticide</th>
<th>Total</th>
<th>Mod- Severe Morbidity</th>
<th>Death</th>
<th>Total</th>
<th>Mod- Severe Morbidity</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrethroids</td>
<td>17,589</td>
<td>778</td>
<td>1</td>
<td>28,362</td>
<td>878</td>
<td>1</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>9,501</td>
<td>567</td>
<td>8</td>
<td>2,921</td>
<td>159</td>
<td>3</td>
</tr>
<tr>
<td>Carbamates</td>
<td>3,750</td>
<td>167</td>
<td>1</td>
<td>1,661</td>
<td>73</td>
<td>1</td>
</tr>
<tr>
<td>Strychnine</td>
<td>134</td>
<td>17</td>
<td>1</td>
<td>66</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Paraquat</td>
<td>77</td>
<td>12</td>
<td>3</td>
<td>90</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Boric Acid</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6,071</td>
<td>12</td>
<td>0</td>
</tr>
</tbody>
</table>

**Report of Poison Control Centers’ National Poison Data System**


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### Data Collection of an Acutely Exposed Patient
Data Collection on an Acute Pesticide Exposed Patient

- **Pesticide Label and/or Safety Data Sheet (SDS)**
- **A fresh urine sample**
- **Copy of pesticide application record**
- **Any contaminated clothing**
- **10 cc whole blood, anticoagulated with sodium heparin**
- **5 cc plasma anticoagulated with sodium heparin**
- **Other options**
  - Fingernail Residue
  - Saliva Sample
  - Hair Sample
  - Skin wipe
Are we done yet?

I am required to report the following:
Pesticide Reporting and Workers' Compensation Information for Hawaii

Report Exposure

Phone: 1-800-222-1222 (Hawaii Poison Control Center)
Report Online: http://eha-web.doh.hawaii.gov/eha-cma/Leaders/HEER/Pesticide-Illness-Reporting

Pesticide Reporting Requirements

Required to Report: Yes

What to Report?: Any Pesticide-Related Exposure
Timeframe to Report Injury or Exposure: 24 Hours
Who is Required to Report?: Physicians, Laboratories.

Additional Info:

For reporting purposes, pesticide and heavy metal poisoning include acute poisoning or any subacute illness caused by, or believed to be caused by, these toxic agents. Alternative Method: 1. Report by phone to the Hawaii Department of Health 1 (800) 586-4249 on O‘ahu, or 1-800-468-4644 ext 64248 if from the Neighbor Islands. 2. Fill out form from web site and mail to the Hawaii Department of Health.

WPS Enforcement

Worker Protection Standard Enforcement Agency:

Department of Agriculture: http://hawaii.gov/hdoa/pl/pest
Workers Compensation

- Medical treatment for injured patient
  - Immediate
  - Long term
  - Access to Specialty Care
- Wages
- Return to Work
- Prevention - Hazard Control
- Public Health
  - Surveillance
When is illness or injury work related?

Any injury or illness resulting from or sustained in the course of any occupation or employment.

More than 50% likely due to work

USE THESE WORDS:

- “More likely than not” due to work
- Work “most likely” cause of the condition
- “But for the work” the condition would not exist

Biomonitoring Data from CDC
Urinary Pesticide Metabolites in Children
2001-2002 National Health and Nutrition Examination Survey (NHANES)

- Pesticide usage questions
  - Use of pesticide in the last month
  - Performed by professional or non-professional

- Dietary questions
  - Intake of types of foods (greens, dried beans)

- Lab data of urinary metabolites of OP and pyrethroid insecticides
  - Age for survey variables limited to 6-18 years to maintain consistency with lab data

Organophosphate Metabolites
(Found in children’s urine)

Chlorpyrifos
Parathion
Methyl parathion
Malathion

- Diethylphosphate
- Diethylthiophosphate
- Paranitrophenol
- Dimethylphosphate
- Dimethylthiophosphate
- Dimethyldithiophosphate
- 3,5,6 Trichloropyridinol
Pyrethroid Metabolites (Found in children’s urine)

- Cypermethrin
- Deltamethrin
- 3-Phenoxybenzoic acid
- Permethrin

Conclusions

- Urinary metabolites of pesticides are higher when:
  - Pesticides have been applied in the past month
  - When applied by a non professional
  - Are applied more often
- Poverty and black race associated with higher organophosphate levels
Chapter 21 - Chronic Effects

- Increasing information about Chronic effects
  - Neurodevelopmental
    - Growing body of solid longitudinal studies
    - Insecticides (OP) affect memory, cognitive development, reasoning, and IQ
  - Birth Defects
    - Some evidence to suggest association
  - Cancer
    - Childhood ALL
    - Prostate cancer and NHL
Pesticides and Childhood Cancer

- Leukemia and brain tumors have been noted in many epidemiological studies to be associated with pesticides
- Risk factors
  - parental occupational exposure
  - family use-- pest strips, termite treatment, flea collars for pets
  - Parental exposure to pesticides BEFORE and DURING pregnancy
- Multiple studies
  - Two important review articles

Adult Cancers
Hodgkins and NHL

- 23 of 27 studies with positive associations\(^1\)
  - Half of studies in farm worker populations
  - Multiple classes of pesticides
- Separate meta-analysis case control studies\(^2\)
  - NHL OR= 1.35, 95% CI, 1.2-1.5
  - Leukemia OR= 1.35, 95% CI, 0.9-1.2
  - Multiple myeloma OR= 1.16, 95% CI, 0.99-1.36

\(^2\)Merhi M, Cancer Causes Control. Dec 2007;18(10):1209-1226

So what do we do?

- Recognize your patient’s occupation
- Recognize and treat acute poisoning
- Report
- Promote primary prevention
- Ask about take home exposures
- Become involved in local/state/federal policy

Summary
• Pesticides may have both Acute and/or Chronic effects
  – Higher short term exposure most often associated with Acute effects
  – Chronic effects may occur as late occurrence following a high exposure, or sub-acute exposure

• Acute effects may often be non-specific
  – Helpful patterns or unique symptoms
  – Needs a high index of suspicion

Resources www.migrantclinician.org
Contact

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